EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	2	("6710184").PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 07:54
S2	2	("4824963").PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 08:04
S3	2	("4503067").PN.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 08:05
S8	330	(548/440).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 08:17
S9	330	(548/444).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 08:17
S10	1011	(514/411).CCLS.	US-PGPUB; USPAT; EPO; DERWENT	OR	OFF	2006/08/30 08:17

```
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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS  4  APR 04   STN AnaVist $500 visualization usage credit offered
 NEWS  5  MAY 10   CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6  MAY 11   KOREAPAT updates resume
 NEWS  7  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 11   CHEMSAFE reloaded and enhanced
 NEWS 14  JUl 14   FSTA enhanced with Japanese patents
 NEWS 15  JUl 19   Coverage of Research Disclosure reinstated in DWPI
 NEWS 16  AUG 09   INSPEC enhanced with 1898-1968 archive
 NEWS 17  AUG 28   ADISCTI Reloaded and Enhanced

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS LOGIN    Welcome Banner and News Items
 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that
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* * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 08:26:29 ON 30 AUG 2006

=> fil reg
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:26:46 ON 30 AUG 2006
```

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STRUCTURE FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3
DICTIONARY FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3

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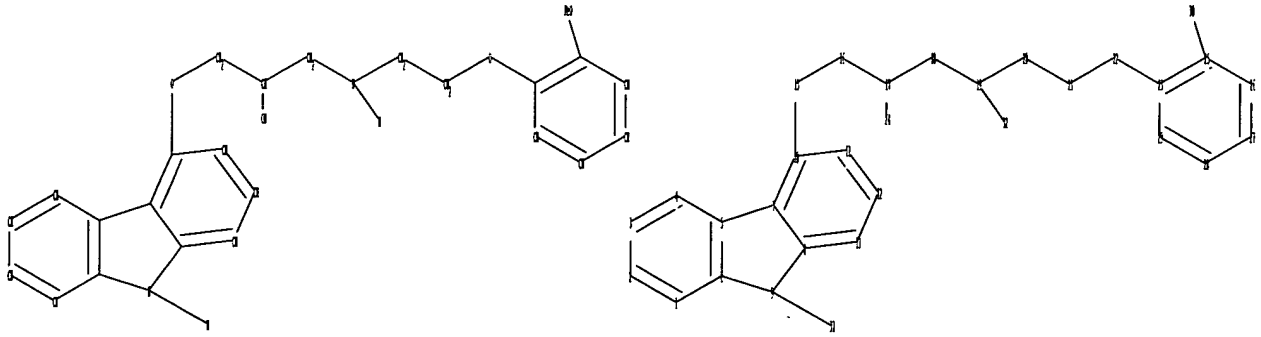
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

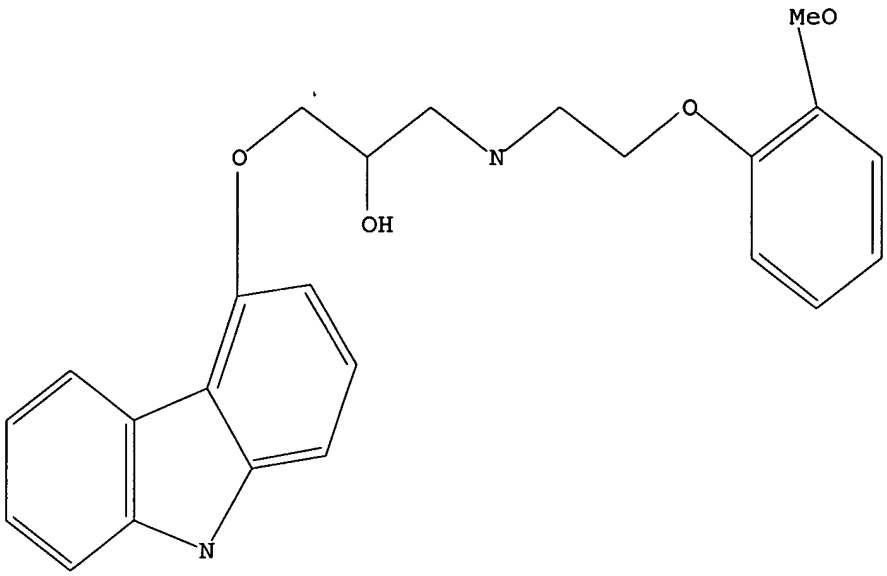
=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10712799.str



chain nodes :
15 16 17 18 19 20 21 22 24 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 23 25 26 27 28 29
chain bonds :
9-31 10-15 15-16 16-17 17-18 17-24 18-19 19-20 19-32 20-21 21-22 22-23
25-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 12-13
23-25 23-29 25-26 26-27 27-28 28-29
exact/norm bonds :
6-9 8-9 10-15 17-24 22-23
exact bonds :
5-7 9-31 15-16 16-17 17-18 18-19 19-20 19-32 20-21 21-22 25-30
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-10 8-13 10-11 11-12 12-13 23-25 23-29
25-26 26-27 27-28 28-29
isolated ring systems :
containing 1 : 23 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom
29:Atom 30:CLASS 31:CLASS 32:CLASS

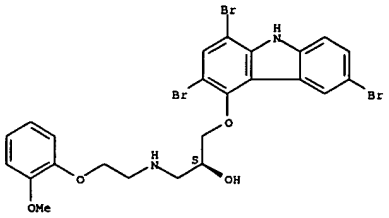
```
L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR
```




```
Structure attributes must be viewed using STN Express query preparation.


=> s l1
SAMPLE SEARCH INITIATED 08:27:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        7 TO ITERATE

100.0% PROCESSED        7 ITERATIONS                                 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            7 TO      298
PROJECTED ANSWERS:               4 TO      200

L2            4 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 08:27:10 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      263 TO ITERATE

100.0% PROCESSED      263 ITERATIONS                               128 ANSWERS
SEARCH TIME: 00.00.01

L3          128 SEA SSS FUL L1

=> d scan
```

L3 128 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN
IN 2-Propanol, 1-[[2-(2-methoxyphenoxy)ethyl]amino]-3-[(1,3,6-tribromo-9H-carbazol-4-yl)oxy]-, (S)- (9CI)
MF C24 H23 Br3 N2 O4

Absolute stereochemistry.



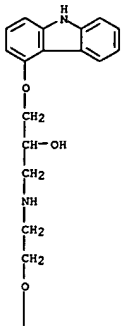
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

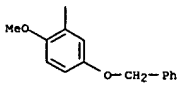
```
=> s l3 and caplus/lc
      51828949 CAPLUS/LC
L4          123 L3 AND CAPLUS/LC

=> s l3 not l4
L5            5 L3 NOT L4

=> d l5 1-5
```

L5 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 887353-00-6 REGISTRY
ED Entered STN: 11 Jun 2006
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-[2-methoxy-5-(phenylmethoxy)phenoxy]ethyl]amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H32 N2 O5
SR Chemical Library

PAGE 1-A



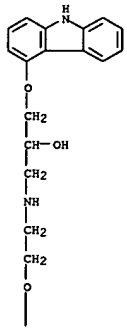
PAGE 2-A



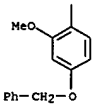
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 887352-95-6 REGISTRY
ED Entered STN: 11 Jun 2006
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-[2-methoxy-4-(phenylmethoxy)phenoxy]ethyl]amino]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C31 H32 N2 O5
SR Chemical Library

PAGE 1-A



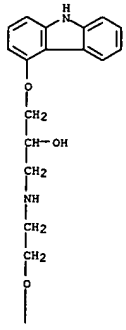
PAGE 2-A



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L5 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-49-9 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol, 4-[(2R)-2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propoxy]- (9CI) (CA INDEX NAME)
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A

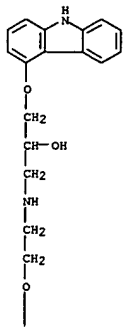


PAGE 2-A

D1—OH

L5 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-20-6 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol, 4-[(2S)-2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propoxy]- (9CI) (CA INDEX NAME)
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A

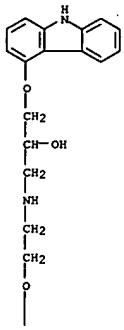


PAGE 2-A

D1—OH

L5 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-15-9 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol, 4-[2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propoxy]-
(9CI) (CA INDEX NAME)
DR 216982-23-9
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A



PAGE 2-A

D1—OH

```
=> fil caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                       182.08     182.29

FILE 'CAPLUS' ENTERED AT 08:28:25 ON 30 AUG 2006
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FILE COVERS 1907 - 30 Aug 2006  VOL 145 ISS 10
FILE LAST UPDATED: 29 Aug 2006  (20060829/ED)

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=> d
YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:n


=> d his

     (FILE 'HOME' ENTERED AT 08:26:29 ON 30 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 08:26:46 ON 30 AUG 2006
L1              STRUCTURE UPLOADED
L2            4 S L1
L3          128 S L1 FULL
L4          123 S L3 AND CAPLUS/LC
L5            5 S L3 NOT L4

     FILE 'CAPLUS' ENTERED AT 08:28:25 ON 30 AUG 2006

=> s l4
L6         1325 L4

=> fil stnguide
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         1.84     184.13

FILE 'STNGUIDE' ENTERED AT 08:31:01 ON 30 AUG 2006
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
```

LAST RELOADED: Aug 25, 2006 (20060825/UP).

=> fil reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.12	184.25

FILE 'REGISTRY' ENTERED AT 08:32:05 ON 30 AUG 2006
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STRUCTURE FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3
DICTIONARY FILE UPDATES: 29 AUG 2006 HIGHEST RN 905300-98-3

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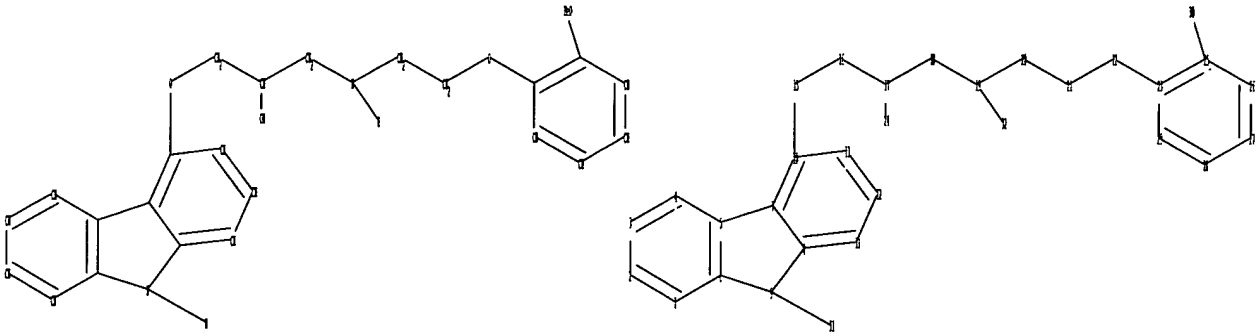
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

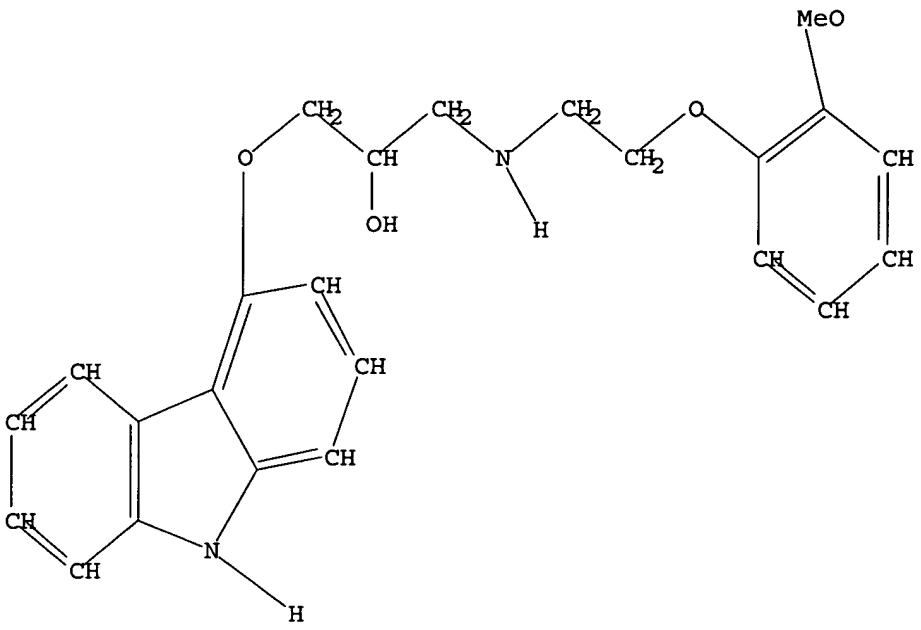
http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\QUERIES\10712799.str



chain nodes :
15 16 17 18 19 20 21 22 24 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 23 25 26 27 28 29
chain bonds :
9-31 10-15 15-16 16-17 17-18 17-24 18-19 19-20 19-32 20-21 21-22 22-23
25-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 12-13
23-25 23-29 25-26 26-27 27-28 28-29

```
exact/norm bonds :
6-9  8-9  10-15  17-24  22-23
exact bonds :
5-7  9-31  15-16  16-17  17-18  18-19  19-20  19-32  20-21  21-22  25-30
normalized bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-10  8-13  10-11  11-12  12-13  23-25  23-29
25-26  26-27  27-28  28-29
isolated ring systems :
containing 1 : 23 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS  22:CLASS  23:Atom  24:CLASS  25:Atom  26:Atom  27:Atom  28:Atom
 29:Atom  30:CLASS  31:CLASS  32:CLASS



L7      STRUCTURE UPLOADED

=> d his

     (FILE 'HOME' ENTERED AT 08:26:29 ON 30 AUG 2006)

     FILE 'REGISTRY' ENTERED AT 08:26:46 ON 30 AUG 2006
L1              STRUCTURE UPLOADED
L2            4 S L1
L3          128 S L1 FULL
L4          123 S L3 AND CAPLUS/LC
L5            5 S L3 NOT L4

     FILE 'CAPLUS' ENTERED AT 08:28:25 ON 30 AUG 2006
L6         1325 S L4

     FILE 'STNGUIDE' ENTERED AT 08:31:01 ON 30 AUG 2006

     FILE 'REGISTRY' ENTERED AT 08:32:05 ON 30 AUG 2006
L7              STRUCTURE UPLOADED

=> d l7
L7 HAS NO ANSWERS
L7              STR
```

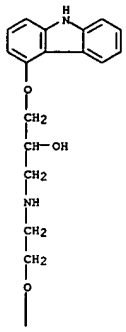


Structure attributes must be viewed using STN Express query preparation.

```
=> s l7 subset=l3 full
FULL SUBSET SEARCH INITIATED 08:32:35 FILE 'REGISTRY'
FULL SUBSET SCREEN SEARCH COMPLETED -      128 TO ITERATE

100.0% PROCESSED      128 ITERATIONS                                57 ANSWERS
SEARCH TIME: 00.00.01

L8            57 SEA SUB=L3 SSS FUL L7

=> s l8 and caplus/lc
      51828949 CAPLUS/LC
L9           54 L8 AND CAPLUS/LC

=> s l8 not l9
L10           3 L8 NOT L9

=> d l10 1-3
```

L10 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-49-9 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol,
4-[(2R)-2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propo
xy]- (9CI) (CA INDEX NAME)
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A



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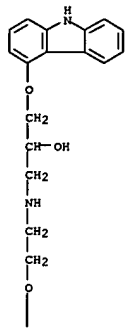
D1—OH

L10 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-20-6 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol,
4-[(2S)-2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propo
xy]- (9CI) (CA INDEX NAME)
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A

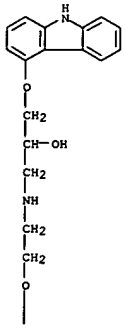


PAGE 2-A

D1—OH

L10 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2006 ACS on STN
RN 216982-15-9 REGISTRY
ED Entered STN: 13 Jan 1999
CN 9H-Carbazolol, 4-[2-hydroxy-3-[[2-(2-methoxyphenoxy)ethyl]amino]propoxy]-
(9CI) (CA INDEX NAME)
DR 216982-23-9
MF C24 H26 N2 O5
CI IDS, COM
SR CA

PAGE 1-A



PAGE 2-A

D1—OH

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	50.74	234.99

FILE 'CAPLUS' ENTERED AT 08:33:21 ON 30 AUG 2006
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FILE COVERS 1907 - 30 Aug 2006 VOL 145 ISS 10
FILE LAST UPDATED: 29 Aug 2006 (20060829/ED)

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=> d his

```
=> s l11 and XRDP
             8 XRDP
L13          0 L11 AND XRDP

=> s l11 and xray
          4489 XRAY
            34 XRAYS
          4522 XRAY
                 (XRAY OR XRAYS)
L14          0 L11 AND XRAY

=> s l11 and x-ray
       1534300 X
       1035920 RAY
        219432 RAYS
       1114901 RAY
                 (RAY OR RAYS)
        821568 X-RAY
                 (X(W)RAY)
L15          5 L11 AND X-RAY

=> d ibib abs hitstr 1-5
```

L15 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1043923 CAPLUS
DOCUMENT NUMBER: 144:40569
TITLE: Development of novel interpenetrating network gellan gum-poly(vinyl alcohol) hydrogel microspheres for the controlled release of carvedilol
AUTHOR(S): Agnihotri, Sunil A.; Aminabhavi, Tejraj M.
CORPORATE SOURCE: Drug Delivery Division, Center of Excellence in Polymer Science, Karnatak University, Dharwad, India
SOURCE: Drug Development and Industrial Pharmacy (2005), 31(6), 491-503
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

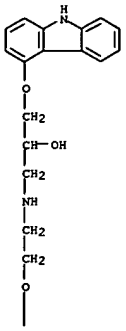
AB Novel interpenetrating polymeric network microspheres of gellan gum and poly(vinyl alc.) were prepared by the emulsion crosslinking method. Carvedilol, an antihypertensive drug, was successfully loaded into these microspheres prepared by changing the exptl. variables such as ratio of gellan gum:poly(vinyl alc.) and extent of crosslinking to optimize the process variables on drug encapsulation efficiency, release rates, size, and morphol. of the microspheres. Formation of interpenetrating network and the chemical stability of carvedilol after preparing the microspheres was confirmed by Fourier transform IR spectroscopy. Differential scanning calorimetry and x-ray diffraction studies were made on the drug-loaded microspheres to investigate the crystalline nature of the drug after encapsulation. Results indicated a crystalline dispersion of carvedilol in the polymer matrix. SEM confirmed the spherical nature and smooth surface morphol. of the microspheres produced. Mean particle size of the microspheres as measured by laser light scattering technique ranged between 230 and 346 μm. Carvedilol was successfully encapsulated up to 87% in the polymeric matrixes. In vitro release studies were performed in the simulated gastric fluid or simulated intestinal fluid. The release of carvedilol was continued up to 12 h. Dynamic swelling studies were performed in the simulated gastric fluid or simulated intestinal fluid, and diffusion coeffs. were calculated by considering the spherical geometry of the matrixes. The release data were fitted to an empirical relation to estimate the transport parameters. The mech. properties of interpenetrating polymeric networks prepared were investigated. Network parameters such as molar mass between cross-links and crosslinking d. for interpenetrating polymeric networks were calculated

IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interpenetrating network gellan gum-poly(vinyl alc.) hydrogel microspheres for controlled release of carvedilol)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L15 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:20485 CAPLUS
DOCUMENT NUMBER: 140:82264
TITLE: Crystalline form of carvedilol hydrobromide for cardiovascular therapy
INVENTOR(S): Chen, Pingyun Y.; Dai, Qunying; Dell'orco, Phillip C.; Hisler, Claire; Igo, David H.; Katrincic, Lee M.; Labaw, Clifford S.; Ping, Li-jen
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002472	A1	20040108	WO 2003-US20346	20030627
WO 2004002472	C1	20050224		
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492084	AA	20040108	CA 2003-2492084	20030627
AU 2003251627	A1	20040119	AU 2003-251627	20030627
EP 1539140	A1	20050615	EP 2003-762148	20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533822	T2	20051110	JP 2004-517980	20030627
US 2005261355	A1	20051124	US 2004-518206	20041216
PRIORITY APPLN. INFO.:			US 2002-392374P	P 20020627
			WO 2003-US20346	W 20030627

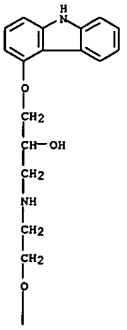
AB The present invention relates to a salt of carvedilol, corresponding compns. containing such a carvedilol salt or corresponding solvates thereof, and/or methods of using the aforementioned compound(s) in the treatment of certain disease states in mammals, in particular man. The present invention further relates to a novel crystalline form of carvedilol hydrobromide, which is the hydrobromide salt of 1-(carbazol-4-yloxy)-3-[[2-(methoxyphenoxy)ethyl]amino]-2-propanol, and/or other carvedilol solvates thereof, compns. containing salts or solvates of carvedilol hydrobromide, and methods of using the aforementioned compound(s) to treat hypertension, congestive heart failure, and angina, etc.

IT 374779-42-7DP, solvates 640724-11-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)

RN 374779-42-7 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide (9CI) (CA INDEX NAME)

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



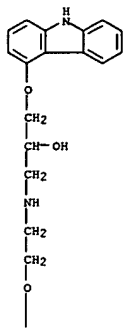
PAGE 2-A

● HBr

RN 640724-11-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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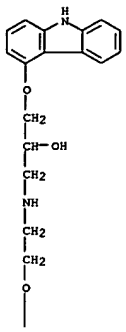
● HBr

● H_2O

IT 374779-42-7
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 374779-42-7 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide (9CI) (CA INDEX NAME)

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



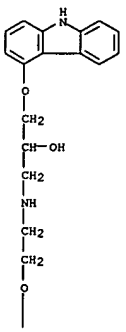
PAGE 2-A

● HBr

IT 72956-09-3, Carvedilol
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrobromination and hydration; crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

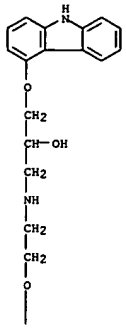
ACCESSION NUMBER: 2001:312052 CAPLUS
DOCUMENT NUMBER: 135:127050
TITLE: Detection of low levels of the amorphous phase in crystalline pharmaceutical materials by thermally stimulated current spectrometry
AUTHOR(S): Venkatesh, Gopi M.; Barnett, Maria E.; Owusu-Fordjour, Charles; Galop, Marc
CORPORATE SOURCE: SB Pharmaceutical, Collegeville, PA, 19426, USA
SOURCE: Pharmaceutical Research (2001), 18(1), 98-103
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Purpose. To demonstrate the applicability of thermally stimulated current (TSC) spectrometry for the detection of low levels of the amorphous phase in crystalline pharmaceutical materials. Methods. A crystalline drug substance was melt quenched to produce an amorphous material. Blends of the crystalline and amorphous phases in different ratios (from 75:25 to 99:01) were prepared by serial dilution TSC studies were performed by applying an elec. field at a temperature above the glass transition temperature (Tg) to orient the dipoles, rapidly cooling to 0°, short circuiting for 1 min. and scanning at 7°/min to measure the depolarization current. The temperature of the peak in the spectrum corresponds to the Tg of the amorphous phase. Modulated DSC studies were performed by using 3 different test protocols (varying linear heating rate, modulation amplitude, and time period). Powder x-ray diffraction (XRD) studies were performed. Results. The ability to detect the amorphous phase by powder XRD is beset with problems due to indirect inference, orientation effects, and instrument-related intensity variations. Even using a consistent sampling procedure and an internal standard, the XRD could quantify the amorphous phase at a level of 5%. In the conventional or modulated DSC, the amorphous phase manifests itself as a shift in the baseline. Using modulated DSC it was possible to detect the amorphous phase at a level of 5% when tested at a heating rate of 2°/min and an amplitude of 1.0° with a period of 30 s. The moisture sorption method appears to have a similar detection capability. In TSC scans, the glass transition event due to mol./segmental mobility in the amorphous phase was manifested as a peak/shoulder on the low-temperature side of the depolarization peak of the crystalline phase. The amorphous phase was unambiguously detected at 2% with a lower detection limit of 1%. Conclusions. On the basis of the results of this preliminary investigation. TSC appears to be capable of detecting the amorphous phase at as low as 1% in crystalline pharmaceuticals, thus offering a much needed capability in discerning factors.

IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of low levels of amorphous phase in crystalline pharmaceuticals

L15 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
by thermally stimulated current spectrometry)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
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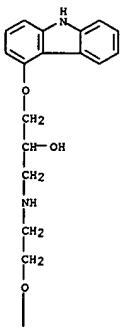
L15 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:810140 CAPLUS
DOCUMENT NUMBER: 130:163115
TITLE: Neuroprotective activities of carvedilol and a hydroxylated derivative. Role of membrane biophysical interactions
AUTHOR(S): Lysko, Paul G.; Lysko, Kathryn A.; Webb, Christine L.; Feuerstein, Giora; Mason, Pamela E.; Walter, Mary F.; Mason, R. Preston
CORPORATE SOURCE: Department of Cardiovascular Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, UW2510, USA
SOURCE: Biochemical Pharmacology (1998), 56(12), 1645-1656
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Carvedilol is a vasodilating β-blocker and antioxidant approved for treatment of mild to moderate hypertension, angina, and congestive heart failure. SB 211475 (4-[2-hydroxyl-3-[[2-(2-methoxyphenoxy)ethyl]amino]propoxyl]-9H-carbazol-3-ol), a hydroxylated carvedilol analog, is an even more potent antioxidant in several assay systems. Carvedilol also has neuroprotective capacity with modulatory actions at N-methyl-D-aspartate (NMDA) receptors and Na+ channels. In the present study, we demonstrated that in cultured rat cerebellar neurons, SB 211475 has 28-fold greater antioxidant activity than carvedilol, but is 2- to 6-fold less potent, resp., at inhibiting neurotoxic activities at Na+ channels and at NMDA receptor channels. To determine a biophys. rationale for these differential activities, small angle x-ray scattering data were obtained from model lipid and brain membrane bilayers containing either carvedilol, SB 211475, or dihydropyridine calcium channel blockers. Electron d. profiles revealed that the location of SB 211475 was restricted to the glycerol backbone/hydrocarbon interface and significantly reduced membrane width by 5%, whereas the time-averaged location for carvedilol and flunarizine also extended to the hydrated surface of the bilayer. Comparison of carvedilol with several dihydropyridines showed a correlation between high ClogP values (lipophilicity), Na+ channel inhibitory potency, and bilayer localization.
The antioxidant activity of SB 211475 could be explained by restricted intercalation into the glycerol phosphate/hydrocarbon interface, creating an increase in volume associated with the phospholipid acyl chains, which would then become resistant to lipid peroxidn. Differential channel modulation may also be explained by these membrane structural results, which indicate that carvedilol and the less spatially restricted dihydropyridine mols. are more likely to inhibit transmembrane receptor channels.
IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroprotective activities of carvedilol and hydroxylated derivative SB 211475 and role of membrane biophys. interactions)
RN 72956-09-3 CAPLUS

L15 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
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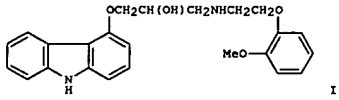
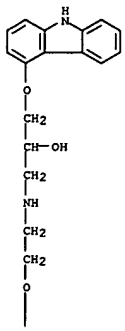
L15 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:654214 CAPLUS
DOCUMENT NUMBER: 130:3743
TITLE: Synthesis and crystal structure of carvedilol
AUTHOR(S): Chen, Wei-Min; Zeng, Long-Mei; Yu, Kai-Bei; Xu, Ji-Hong
CORPORATE SOURCE: Inst. Pharmaceutical Sci., The First Military Med. Univ., Canton, 510515, Peop. Rep. China
SOURCE: Jiegou Huaxue (1998), 17(5), 325-328
CODEN: JHUADF; ISSN: 0254-5861
PUBLISHER: "Jiegou Huaxue" Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The crystal structure of carvedilol (I), prepared from 4-(2,3-epoxypropoxy)carbazole and 2-MeOC6H4OCH2CH2NH2, was determined by single-crystal x-ray diffraction. The crystal is composed of a pair of enantiomers, and there are hydrogen bonds O-H-N between the two enantiomers. There are two planes in the mol.
IT 72956-09-3P, Carvedilol
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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L4             123 S L3 AND CAPLUS/LC
L5               5 S L3 NOT L4

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     FILE 'REGISTRY' ENTERED AT 08:32:05 ON 30 AUG 2006
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L8              57 S L7 FULL SUB=L3
L9              54 S L8 AND CAPLUS/LC
L10              3 S L8 NOT L9

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L15              5 S L11 AND X-RAY

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L18 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:558278 CAPLUS
DOCUMENT NUMBER: 145:62782
TITLE: Process for the preparation of carvedilol or its enantiomers from the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole or its enantiomers with an excess of 2-(2-methoxyphenoxy)ethylamine in ethyl acetate as the reaction solvent
INVENTOR(S): Trepat Guixer, Elisenda; Munoz Alvarez, Anna; Pomares Marco, Marta; Marquillas Olondriz, Francisco
PATENT ASSIGNEE(S): Zambon Group S.p.A., Italy
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006061364	A1	20060615	WO 2005-EP56469	20051205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2004-106438 A 20041209

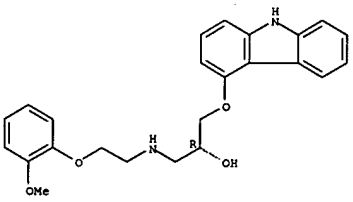
OTHER SOURCE(S): CASREACT 145:62782

AB A process for the preparation of carvedilol, as well as its optically active R and S enantiomers, comprises the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole, or its enantiomers, with an excess of 2-(2-methoxyphenoxy)ethylamine using Et acetate as the reaction solvent.

IT 72956-09-3P, Carvedilol 95093-99-5P, (R)-Carvedilol 95094-00-1P, (S)-Carvedilol
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of carvedilol or its enantiomers from the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole or its enantiomers with an excess of 2-(2-methoxyphenoxy)ethylamine in Et acetate as the reaction solvent)

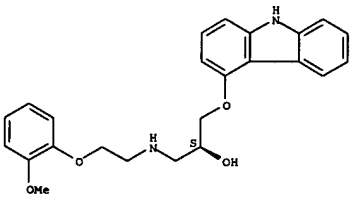
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

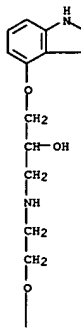
Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 1 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L18 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1134485 CAPLUS
DOCUMENT NUMBER: 143:353578
TITLE: Validation of UV spectrophotometric and nonaqueous titration methods for the determination of carvedilol in pharmaceutical formulations
AUTHOR(S): Ieggli, Carine Viana Silva; Cardoso, Simone Goncalves; Belle, Luziane Potrich
CORPORATE SOURCE: Universidade Federal de Santa Maria, Departamento de Farmacia Industrial, Santa Maria, CEP 97105-900, Brazil
SOURCE: Journal of AOAC International (2005), 88(5), 1299-1303
CODEN: JAINEE; ISSN: 1060-3271
PUBLISHER: AOAC International
DOCUMENT TYPE: Journal
LANGUAGE: English

AB UV spectrophotometric and nonaq. volumetric methods are described for the determination of carvedilol in pharmaceutical formulations. Linearity, precision, and accuracy were evaluated according to the validation guidelines of the International Conference on Harmonization and the USP for both methods. The UV spectrophotometric procedure was performed in ethanol at 244 nm. Good linearity was obtained between 2 and 7 μg/mL with a correlation coefficient of 0.9999. The intra- and interday precision values were <2% for all samples analyzed. The accuracy, determined from recovery studies, was between 97.5 and 102.2%. The other procedure was based on the volumetric quantitation of carvedilol in a nonaq. medium with 0.01M perchloric acid and 1% violet crystal as the indicator. The validation of the volumetric method yielded good results that included linearity (r of >0.999), precision (relative standard deviations of <2% for intra- and interday precision), and accuracy (96.4-102.4%). The methods were applied to tablets and compounded capsules. Statistical anal. by anal. of variance showed no significant difference between the results obtained by the proposed methods.

IT 72956-09-3, Carvedilol
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(UV spectrophotometry and nonaq. titration for determination of carvedilol in pharmaceutical formulations)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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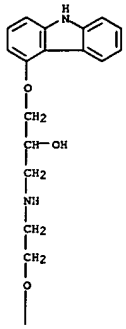

PAGE 2-A

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L18 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1043923 CAPLUS
DOCUMENT NUMBER: 144:40569
TITLE: Development of novel interpenetrating network gellan gum-poly(vinyl alcohol) hydrogel microspheres for the controlled release of carvedilol
AUTHOR(S): Agnihotri, Sunil A.; Aminabhavi, Tejraj M.
CORPORATE SOURCE: Drug Delivery Division, Center of Excellence in Polymer Science, Karnatak University, Dharwad, India
SOURCE: Drug Development and Industrial Pharmacy (2005), 31(6), 491-503
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Novel interpenetrating polymeric network microspheres of gellan gum and poly(vinyl alc.) were prepared by the emulsion crosslinking method. Carvedilol, an antihypertensive drug, was successfully loaded into these microspheres prepared by changing the exptl. variables such as ratio of gellan gum:poly(vinyl alc.) and extent of crosslinking to optimize the process variables on drug encapsulation efficiency, release rates, size, and morphol. of the microspheres. Formation of interpenetrating network and the chemical stability of carvedilol after preparing the microspheres was confirmed by Fourier transform IR spectroscopy. Differential scanning calorimetry and x-ray diffraction studies were made on the drug-loaded microspheres to investigate the crystalline nature of the drug after encapsulation. Results indicated a crystalline dispersion of carvedilol in the polymer matrix. SEM confirmed the spherical nature and smooth surface morphol. of the microspheres produced. Mean particle size of the microspheres as measured by laser light scattering technique ranged between 230 and 346 μm. Carvedilol was successfully encapsulated up to 87% in the polymeric matrixes. In vitro release studies were performed in the simulated gastric fluid or simulated intestinal fluid. The release of carvedilol was continued up to 12 h. Dynamic swelling studies were performed in the simulated gastric fluid or simulated intestinal fluid, and diffusion coeffs. were calculated by considering the spherical geometry of the matrixes. The release data were fitted to an empirical relation to estimate the transport parameters. The mech. properties of interpenetrating polymeric networks prepared were investigated. Network parameters such as molar mass between cross-links and crosslinking d. for interpenetrating polymeric networks were calculated

IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interpenetrating network gellan gum-poly(vinyl alc.) hydrogel microspheres for controlled release of carvedilol)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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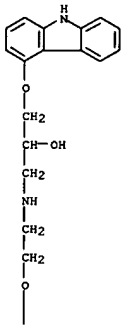

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REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L18 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:638703 CAPLUS
DOCUMENT NUMBER: 143:139194
TITLE: Buccal dosage forms for extended drug release
INVENTOR(S): Jain, Rajesh; Jindal, Kour Chand; Singh, Sukhjeet
PATENT ASSIGNEE(S): Panacea Biotec Ltd., India
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005065640	A1	20050721	WO 2005-IN3	20050105
WO 2005065640	C1	20051208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2004-DE24 A 20040106
IN 2004-DE26 A 20040106

AB Buccal dosage form compns., preferably of poorly bioavailable drug(s), or drug(s) which undergo extensive presystematic metabolism, are provided. The compns. provide extended release of the drug in the oral cavity, and are preferably in the taste masked form. A process of preparing of such compns. is also provided. Thus, a tablet contained sumatriptan succinate 25.0, Indion-204 75.0, maltodextrin 48.0, sucrose 30.0, CM-cellulose 18.0, HPMC 8.0, HPC 8.0, citric acid 15.0, NaCl 5.0, and Povidone 3.0 25 mg/tablet.

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal dosage forms for extended drug release)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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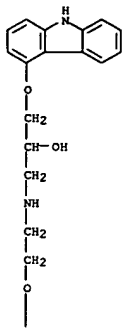

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REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:493479 CAPLUS
DOCUMENT NUMBER: 143:32328
TITLE: Carvedilol free base, salts and solvates for controlled release formulations for treatment of cardiovascular diseases
INVENTOR(S): Burke, Matthew D.; Lamey, Kimberly A.; Martini, Luigi G.; Oh, Choon; Peterson, Heather; Staton, Jeffrey Scott; Zhang, Lihua; Coffin, Mark Davis
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 248 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051325	A2	20050609	WO 2004-US39677	20041124
WO 2005051325	A3	20050811		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1686967	A2	20060809	EP 2004-812238	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				

PRIORITY APPLN. INFO.: US 2003-524991P P 20031125
WO 2004-US39677 W 20041124

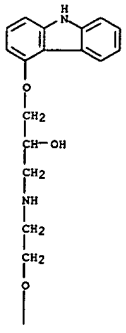
AB The present invention relates to carvedilol free base, salts, anhydrous forms, or solvates thereof, corresponding pharmaceutical compns. or controlled release formulations, and methods for delivery of carvedilol forms to the lower gastrointestinal tract or methods to treat cardiovascular diseases, which may include, but are not limited to hypertension, congestive heart failure, and angina. Thus, carvedilol monocitrate monohydrate was prepared by reaction of 100 g 20% citric acid solution and 2.2 g carvedilol and overnight evaporation giving large single crystals. Also, controlled-release carvedilol tablets were prepared by spray coating a core. The core comprised carvedilol phosphate hemihydrate 41.4, mannitol 261.6,, Hypromellose 120.4, microcryst. cellulose 120.6, Povidone 47, colloidal silica 6.0, and Mg stearate 6.0 mg. The cores were spray coated by an aqueous suspension containing (per tablet) Opadry II Color 12.1, Eudragit L30 D-55 39.2, tri-Et citrate 4.0, glyceryl stearate 1.3, and Polysorbate 80 4.0 mg.

IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral controlled-release carvedilol free base and salts and solvates

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
for in treatment of cardiovascular diseases)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

IT 340269-63-8P 374779-41-6P 374779-42-7P
374779-43-8P 374779-45-0P 374779-53-0P
374779-87-0P 610309-89-2P 623113-70-2P
640724-11-4P 641571-35-9P 787598-89-4P,
Carvedilol oxalate 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P
852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P 852995-90-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oral controlled-release carvedilol free base and salts and solvates for in treatment of cardiovascular diseases)

RN 340269-63-8 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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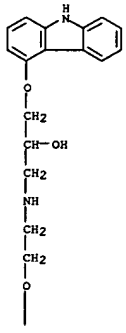


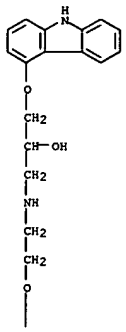
PAGE 2-A

CM 2

CRN 75-75-2
CMF C H4 O3 S

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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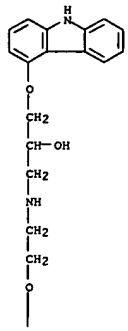
● HCl

RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HBr

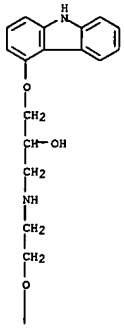
RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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CM 2

CRN 7664-93-9
CMF H2 O4 S

RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

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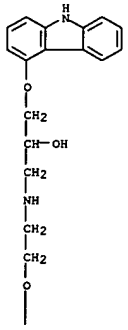

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CM 2

CRN 7664-38-2
CMF H3 O4 P

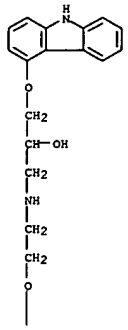
RN 374779-53-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

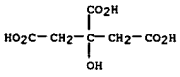
PAGE 1-A



PAGE 2-A

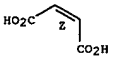
CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 374779-87-0 CAPLUS

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

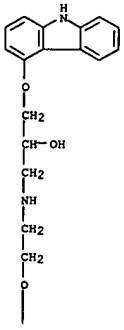


RN 610309-89-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino}-,
phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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CM 2

CRN 7664-38-2

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino}-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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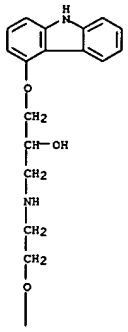

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CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CMF H3 O4 P

RN 623113-70-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino}-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI)
(CA
INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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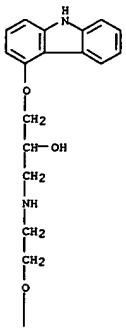

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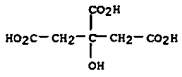
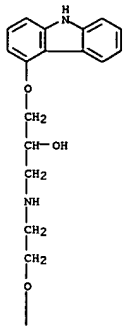
CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



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● HBr

● H_2O

RN 641571-35-9 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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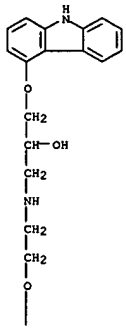

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CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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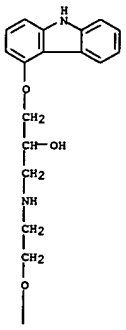


PAGE 2-A

CM 2

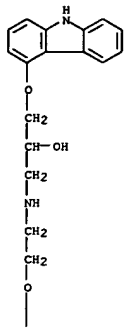
CRN 144-62-7
CMF C2 H2 O4

RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-
3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX
NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

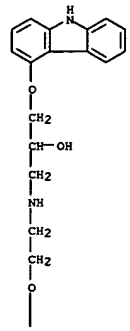
CRN 90-64-2
CMF C8 H8 O3

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

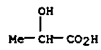
PAGE 1-A



PAGE 2-A

CM 2

CRN 50-21-5
CMF C3 H6 O3

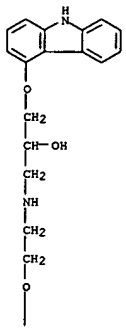


CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

CM 2

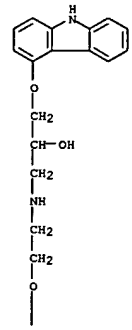
CRN 110-94-1
CMF C5 H8 O4

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

RN 852995-81-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino)-, monobenzoate (salt) (9CI) (CA INDEX NAME)

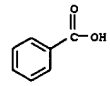
PAGE 1-A



PAGE 2-A

CM 2

CRN 65-85-0
CMF C7 H6 O2



CM 1

RN 852995-82-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

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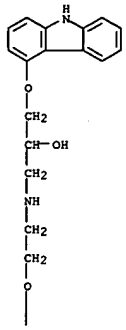


PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:7) (9CI) (CA INDEX NAME)

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CM 3

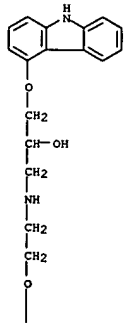
CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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CM 2

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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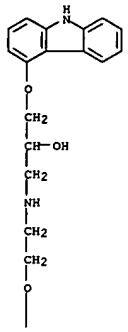

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CM 2

CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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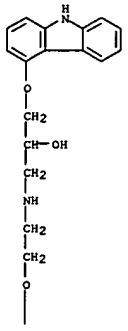


PAGE 2-A

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

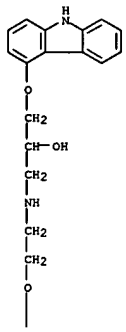
CRN 71-41-0
CMF C5 H12 O

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A

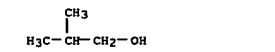


PAGE 2-A

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 78-83-1
CMF C4 H10 O



RN 852995-87-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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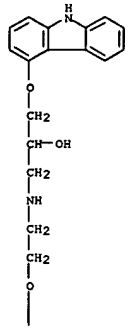
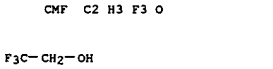


PAGE 2-A

L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 75-89-8
CMF C2 H3 F3 O



RN 852995-88-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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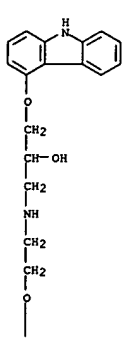

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L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 67-63-0
CMF C3 H8 O

RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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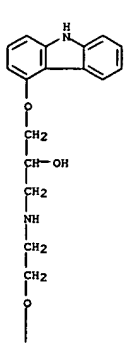

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L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 71-23-8
CMF C3 H8 O

RN 852995-90-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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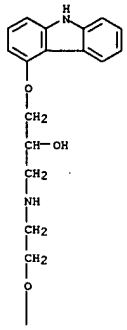


PAGE 2-A

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:490290 CAPLUS
DOCUMENT NUMBER: 143:32320
TITLE: Carvedilol salts and solvates and corresponding compositions for treatment of cardiovascular diseases
INVENTOR(S): Brook, Christopher S.; Chen, Pingyun Y.; Chen, Wei; Dai, Qunying; Dell'Orco, Philip C.; Hisler, Claire; Igo, David H.; Katrincic, Lee M.; Labaw, Clifford S.; Louvet, Ann Marie; Oh, Choon K.; Ping, Li-Jen; Spoors, Paul G.; Wang, Jun; Werner, Christopher
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., USA
SOURCE: PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051383	A1	20050609	WO 2004-US39528	20041124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005277689	A1	20051215	US 2004-997230	20041124
EP 1686986	A1	20060809	EP 2004-812113	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				

PRIORITY APPLN. INFO.: US 2003-524921P P 20031125
WO 2004-US39528 W 20041124

AB The present invention relates to a salt of carvedilol and/or corresponding solvates thereof, compns. containing such carvedilol and/or corresponding solvates thereof, and/or methods of using the aforementioned compound(s) in the treatment of certain disease states in mammals, in particular man. The present invention further relates to carvedilol phosphate salts, and/or solvates thereof, which include a novel crystalline form of carvedilol dihydrogen phosphate, and/or carvedilol hydrogen phosphate, and/or other corresponding solvates thereof, compns. containing these carvedilol salts and/or solvates, and methods of using these compds. to treat hypertension, congestive heart failure, angina, etc. Thus, carvedilol dihydrogen phosphate hemihydrate Form I was prepared from a reaction mixture of carvedilol and H3PO4 in acetone by adding seeds of carvedilol dihydrogen phosphate. Also, the pharmacokinetic study in dogs showed that oral bioavailability from carvedilol base in the small intestine is constrained by its low solubility at neutral pH. When oral units were introduced to the stomach, the low gastric pH can be expected to facilitate dissoln. and absorption but this will not be the case in the more neutral small intestine or beyond. Thus, salts of carvedilol (carvedilol hydrobromide, phosphate and citrate) were formulated by using conventional (non-solubilizing) excipients such that drug did not become available until units were beyond the gastric milieu. Drug administered in salt form was rapidly and more completely absorbed than the free base form.

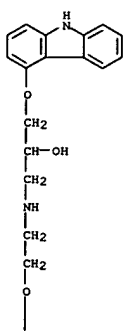
IT 340269-63-8P 374779-41-6P 374779-42-7P
374779-43-8P 374779-45-0P 374779-53-0P
374779-87-0P 610309-89-2P 623113-70-2P
640724-11-4P 641571-35-9P 787598-89-4P,
Carvedilol oxalate 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P
852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P 852995-90-5P
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(carvedilol salts and solvates for oral compns. with improved bioavailability for treatment of cardiovascular diseases)

RN 340269-63-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



L18 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 64-17-5
CMF C2 H6 O

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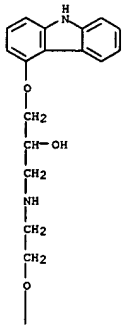
CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



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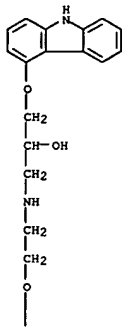
● HCl

RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



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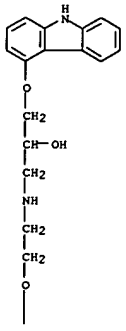
● HBr

RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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CM 2

CRN 7664-93-9
CMF H2 O4 S

RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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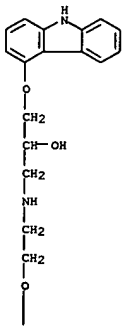

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CM 2

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

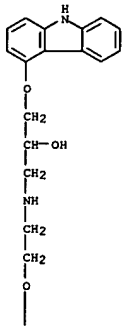
CRN 7664-38-2
CMF H3 O4 P

RN 374779-53-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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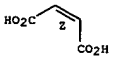
CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



RN 610309-89-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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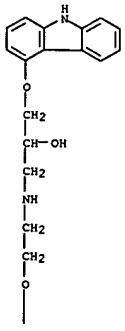
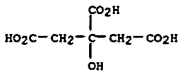


L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 77-92-9
CMF C6 H8 O7

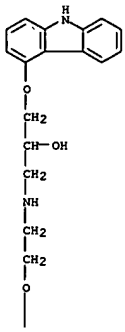


RN 374779-87-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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CM 2

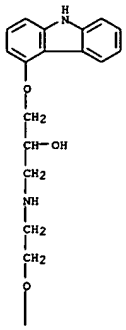
CRN 7664-38-2
CMF H3 O4 P

RN 623113-70-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI) (CA
INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

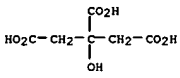
PAGE 1-A



PAGE 2-A

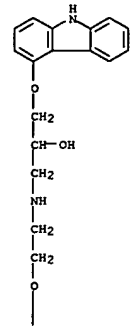
CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



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● HBr

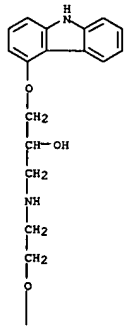
● H_2O

RN 641571-35-9 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

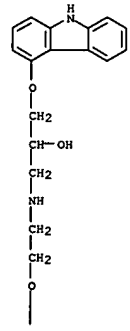
CRN 7664-38-2
CMF H3 O4 P

RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

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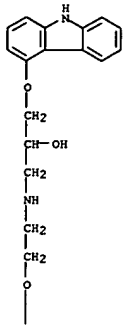

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CM 2

CRN 90-64-2
CMF C8 H8 O3

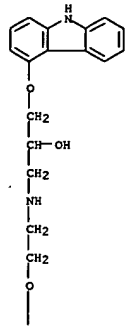
RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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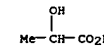
CM 2

CRN 50-21-5
CMF C3 H6 O3



RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

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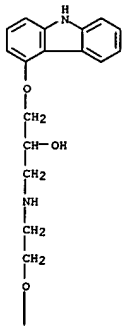
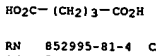


PAGE 2-A

CM 2

CRN 110-94-1
CMF C5 H8 O4



RN 852995-81-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

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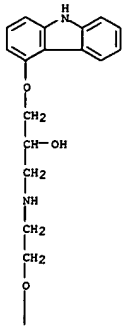

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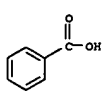
CM 2

CRN 65-85-0
CMF C7 H6 O2



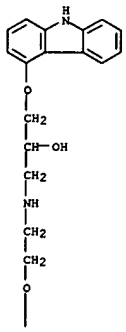
RN 852995-82-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 3

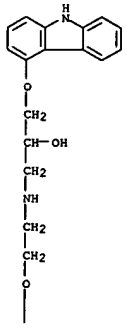
CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A

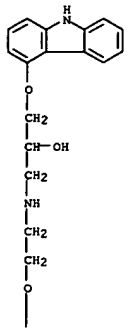


L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

CM 2

CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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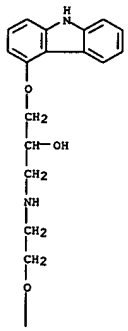


PAGE 2-A

CM 2

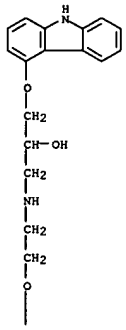
CRN 71-41-0
CMF C5 H12 O

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

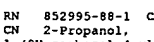
PAGE 1-A



PAGE 2-A

CM 2

CRN 75-89-8
CMF C2 H3 F3 O



RN 852995-88-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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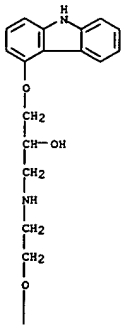
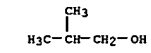


PAGE 2-A

CM 2

CRN 78-83-1
CMF C4 H10 O

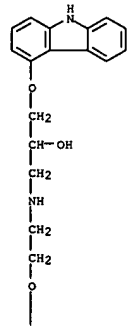


RN 852995-87-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

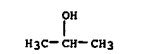
PAGE 1-A



PAGE 2-A

CM 2

CRN 67-63-0
CMF C3 H8 O



RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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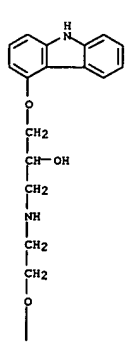


PAGE 2-A

CM 2

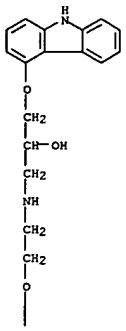
CRN 71-23-8
CMF C3 H8 O

RN 852995-90-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

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CM 2

CRN 64-17-5
CMF C2 H6 O

IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(carvedilol salts and solvates for oral compns. with improved bioavailability for treatment of cardiovascular diseases)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

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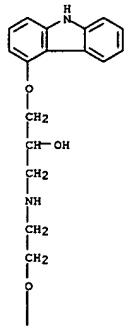

ACCESSION NUMBER: 2005:490272 CAPLUS
DOCUMENT NUMBER: 143:48055
TITLE: Controlled release pharmaceuticals containing carvedilol, its salts, or solvates
INVENTOR(S): Castan, Catherine; Crowley, Patrick J.; Guimberteau, Florence; Meyrueix, Remi; Oh, Choon; Soula, Gerard
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.; Flamel Technologies
SOURCE: PCT Int. Appl., 287 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051322	A2	20050609	WO 2004-US39614	20041124
WO 2005051322	A3	20060420		
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2547137	AA	20050609	CA 2004-2547137	20041124
US 2005175695	A1	20050811	US 2004-997836	20041124
US 2005196459	A1	20050908	US 2004-996780	20041124
EP 1691789	A2	20060823	EP 2004-812185	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				

PRIORITY APPLN. INFO.:
US 2003-524991P P 20031125
US 2004-605680P P 20040830
WO 2004-US39614 W 20041124

AB The present invention also relates to carvedilol free base, its salts, anhydrous forms, or solvates, corresponding controlled release formulations, and delivery or dosing methods of carvedilol forms to the lower gastrointestinal tract or methods to treat cardiovascular diseases, which may include, but are not limited to hypertension, congestive heart failure, atherosclerosis, and angina. The present invention relates to controlled release formulations, which comprise various carvedilol forms, which may include, but are not limited to a carvedilol free base or corresponding carvedilol salts, anhydrous forms or solvates thereof. Thus, carvedilol dihydrogen phosphate dihydrate was prepared by dissolving carvedilol dihydrogen phosphate in acetone/water mixture and removing acetone.

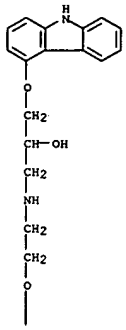
IT 374779-53-0P 623113-70-2P
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation);

L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals contg. carvedilol or its salts or solvates)
RN 374779-53-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

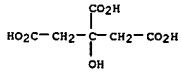
PAGE 1-A



PAGE 2-A

CM 2

CRN 77-92-9
CMF C6 H8 O7



IT 72956-09-3
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or solvates)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

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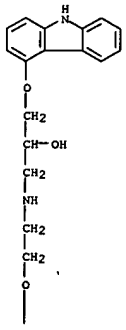

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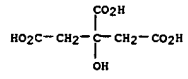
L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

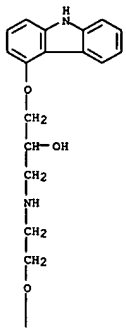


RN 623113-70-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



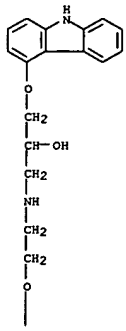
PAGE 2-A

CM 2

L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT 374779-42-7P 640724-11-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or solvates)
RN 374779-42-7 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A

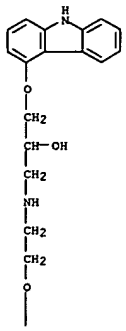


PAGE 2-A

● HBr

RN 640724-11-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

● HBr

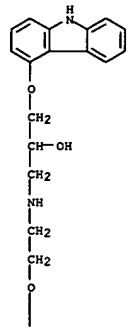
● H_2O

IT 374779-45-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(controlled release pharmaceuticals containing carvedilol or its salts or
solvates)
RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

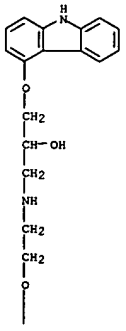
IT 374779-43-8P 374779-87-0P 610309-89-2P
641571-35-9P 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P

852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals contg. carvedilol or its salts or
solvates)
RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-93-9

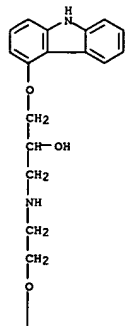
CMF H2 O4 S

RN 374779-87-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A

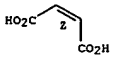


PAGE 2-A

CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

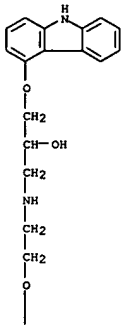


RN 610309-89-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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CM 2

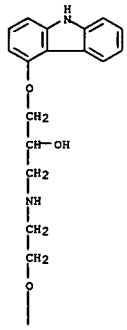
CRN 7664-38-2
CMF H3 O4 P

RN 641571-35-9 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

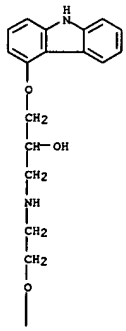
CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



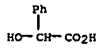
PAGE 1-A



PAGE 2-A

CM 2

CRN 90-64-2
CMF C8 H8 O3



RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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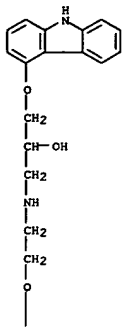

PAGE 2-A

CM 2

CRN 50-21-5
CMF C3 H6 O3

RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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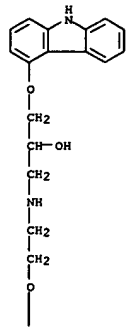
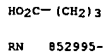


PAGE 2-A

CM 2

CRN 110-94-1
CMF C5 H8 O4



RN 852995-81-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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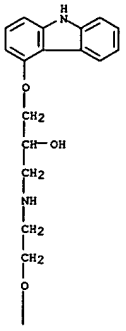
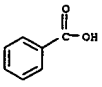


PAGE 2-A

CM 2

CRN 65-85-0
CMF C7 H6 O2

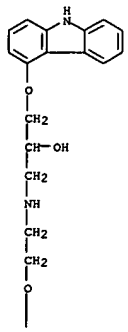


RN 852995-82-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

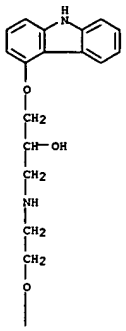
CRN 7664-38-2
CMF H3 O4 P

RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

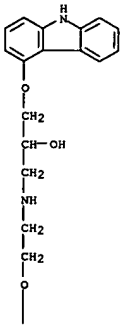
CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 3

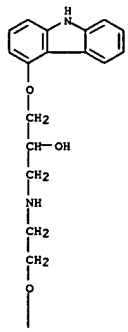
CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CM 2

CRN 71-41-0
CMF C5 H12 O

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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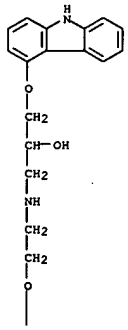
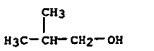


PAGE 2-A

L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 78-83-1
CMF C4 H10 O

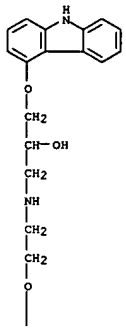


RN 852995-87-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

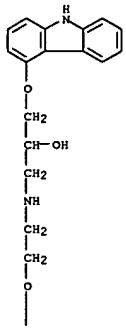
CRN 75-89-8
CMF C2 H3 F3 O

RN 852995-88-1 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A

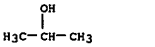


PAGE 2-A

L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 67-63-0
CMF C3 H8 O



RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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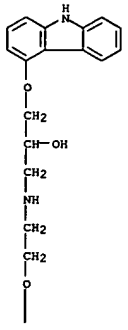

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L18 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

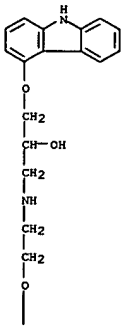
CRN 71-23-8
CMF C3 H8 O

IT 340269-63-8 374779-41-6 787598-89-4,
Carvedilol oxalate 852995-90-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or
solvates)
RN 340269-63-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



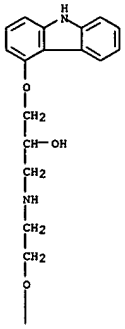
PAGE 2-A

CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

● HCl

RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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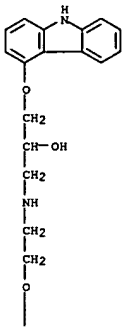

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CM 2

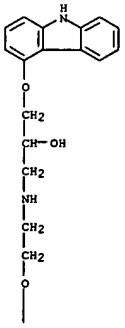
CRN 144-62-7
CMF C2 H2 O4

RN 852995-90-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 64-17-5
CMF C2 H6 O

L18 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:216797 CAPLUS
DOCUMENT NUMBER: 142:285152
TITLE: New crystalline forms of carvedilol
INVENTOR(S): Zupet, Rok; Grcman, Marija; Smrkolj, Matej
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil D.D. Novo Mesto, Slovenia
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021504	A2	20050310	WO 2004-SI29	20040901
WO 2005021504	A3	20050602		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
SI 21616	C	20050430	SI 2003-218	20030902
EP 1660451	A2	20060531	EP 2004-775682	20040901
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: SI 2003-218 A 20030902
WO 2004-SI29 W 20040901

AB The present invention relates to new crystalline carvedilol forms VII and IX and to processes for the preparation Particularly, this invention relates to processes of the isolation of carvedilol, using Et acetate as a solvent and preparation of an Et acetate solvate.

IT 847440-46-4P
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(crystalline forms of carvedilol)

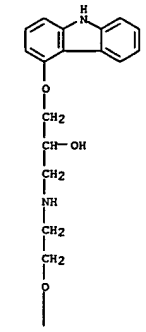
RN 847440-46-4 CAPLUS
CN Acetic acid ethyl ester, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

L18 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

CM 2

CRN 141-78-6
CMF C4 H8 O2

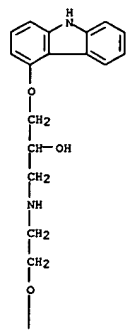
Et—O—Ac

IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(crystalline forms of carvedilol)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

L18 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1154673 CAPLUS
DOCUMENT NUMBER: 142:93675
TITLE: A process for preparation of 1-[9H-carbazol-4-yloxy]-3-[[2-(2-methoxyphenoxy)ethyl]amino]propan-2-ol
INVENTOR(S): Chhabada, Vijay Chhangamal; Rehani, Rajeev Budhdev; Thennati, Rajamannar
PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004113296	A1	20041229	WO 2004-IN52	20040304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: IN 2003-MU647 A 20030620
IN 2003-MU721 A 20030717

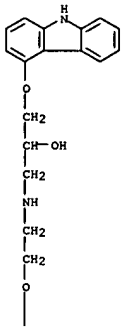
OTHER SOURCE(S): CASREACT 142:93675; MARPAT 142:93675
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention provides a process for preparation of 1-[9H-carbazol-4-yloxy]-3-[[2-(2-methoxyphenoxy)ethyl]amino]-propan-2-ol (I) in racemic form or in the form of optically active R or S enantiomer or its pharmaceutically acceptable salt, comprising, reacting 4-(oxiranylmethoxy)-9H-carbazole (II) or the R or S enantiomer thereof with a compound of formula (III) (wherein R1 = benzyl or substituted benzyl), in an aprotic organic solvent in presence of a catalyst to obtain a compound of formula (IV) (wherein R1 is as defined above), or the R or S enantiomer thereof. The resultant compound IV is subjected to debenzylation reaction by catalytic hydrogenation to obtain the compound I, if desired converting the resultant compound I to a pharmaceutically acceptable salt thereof. Thus, to 400 mL EtOAc, 70 g (0.27 mol) anhydrous N-[2-(2-(methoxy)phenoxy]ethyl]benzylamine, 10.25 g (0.075 mol) anhydrous ZnCl2, and 50 g (0.21 mol) 4-(oxiranylmethoxy)-9H-carbazole were added and the reaction mixture was heated to 70-75° for 3 h (TLC control for checking conversion to N-benzylcarvedilol), cooled to ambient temperature, and

L18 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
quenched into 100 mL 12-15% aq. NH3. The aq. layer was sepd., and the product enriched org. layer was washed with water till neutral Ph, treated
with charcoal, and filtered. To this soln. of N-benzyl carvedilol in EtOAc, 7 g wet 5% Pd/C catalyst (50% moisture content) was added and the reaction mixt. was hydrogenated at 3.5-4.5 Kg/cm2 at temp. 60-70° for a period of about 10 h and filtered. The filtrate was concd. to remove EtOAc. To the resultant syrupy mass n-butanol (100 mL) was added and the soln. was stirred for .apprx.10 h. The crystals were sepd. by filtration, washed successively with n-butanol (50 mL) and toluene (50 mL) to obtain carvedilol (47 g) which was recrystd. from 3 vols. EtOAc to obtain carvedilol (42 g).
IT 72956-09-3P, Carvedilol 95093-99-5P,
(R)-1-(9H-Carbazol-4-yloxy)-3-[[2-[2-(methoxy)phenoxy]ethyl]amino]propan-2-ol 95094-00-1P, (S)-1-(9H-Carbazol-4-yloxy)-3-[[2-[2-(methoxy)phenoxy]ethyl]amino]propan-2-ol
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of carvedilol by amination of oxiranylmethoxycarbazole with
N-(methoxyphenoxyethyl)benzylamine and hydrogenolysis of N-benzylcarvedilol)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A

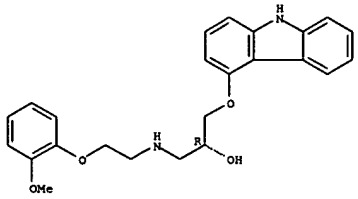


L18 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

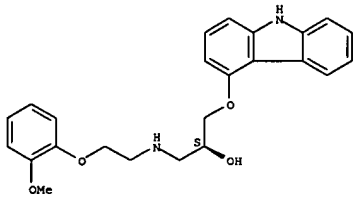
RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

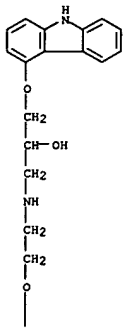
L18 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:927171 CAPLUS
DOCUMENT NUMBER: 141:395415
TITLE: Process for the preparation of crystalline carvedilol form-II
INVENTOR(S): Ramanjaneyulu, Gorantla Seeta; Kumar, Indukuri Venkata
Sunil; Rao, Ketavarapu Narasimha; Kishore, Jammula Vera Venkata Krishna
PATENT ASSIGNEE(S): Matrix Laboratories Ltd., India
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094378	A1	20041104	WO 2004-IN104	20040416
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1615888	A1	20060118	EP 2004-727971	20040416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			IN 2003-MA328	A 20030421
			WO 2004-IN104	W 20040416

OTHER SOURCE(S): CASREACT 141:395415
AB The present invention provides a cost-effective, industrially feasible process for the manufacture of crystalline carvedilol form-II using novel carvedilol salts comprising a step of reacting 4-(2,3-epoxypropoxy)carbazole with 2-(2-methoxyphenoxy)ethylamine followed by acidification with mineral acid in presence of an organic solvent to yield
acid addition salts, (e.g. carvedilol oxalate), treatment of the said salts
with base(s) in presence of organic solvent(s), water, and isolation from the
organic solvent(s) followed by crystallization from Et acetate.
IT 72956-09-3P, Carvedilol
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation of crystalline carvedilol form-II by reaction of 4-(2,3-epoxypropoxy)carbazole with 2-(2-methoxyphenoxy)ethylamine)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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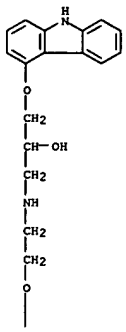
IT 787598-89-4P, Carvedilol oxalate 787598-91-8P, Carvedilol salicylate
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of crystalline carvedilol form-II by reaction of 4-(2,3-epoxypropoxy)carbazole with 2-(2-methoxyphenoxy)ethylamine)
RN 787598-89-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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CM 2

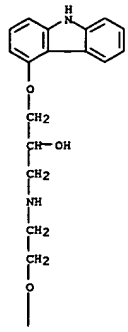
CRN 144-62-7
CMF C2 H2 O4

RN 787598-91-8 CAPLUS
CN Benzoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

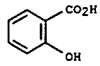
PAGE 1-A



PAGE 2-A

CM 2

CRN 69-72-7
CMF C7 H6 O3



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

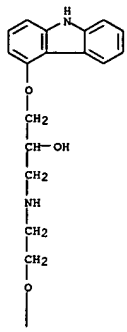
L18 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:412919 CAPLUS
DOCUMENT NUMBER: 140:406735
TITLE: Process for the preparation of carvedilol from 4-(oxirane-2-ylmethoxy)-9H-carbazole and 2-(2-methoxyphenoxy)ethylamine salts
INVENTOR(S): Hercek, Richard; Skoda, Alojz; Proksa, Bohumil
PATENT ASSIGNEE(S): Zentiva, A.S., Slovakia
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041783	A1	20040521	WO 2003-SK20	20031104
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003301861	A1	20040607	AU 2003-301861	20031104
EP 1558575	A1	20050803	EP 2003-810732	20031104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2006167077	A1	20060727	US 2005-533809	20050505
PRIORITY APPLN. INFO.:			SK 2002-1595 A	20021108
			WO 2003-SK20 W	20031104

OTHER SOURCE(S): CASREACT 140:406735
AB Carvedilol is prepared in high yield and selectivity by the reaction of 4-(oxirane-2-ylmethoxy)-9H-carbazole with acid-addition salts of 2-(2-methoxyphenoxy)ethylamine [e.g., 2-(2-methoxyphenoxy)ethylamine hydrochloride] in the presence of a base (e.g., potassium carbonate) in an C2-5 alc. solvent (e.g., isopropanol) at an elevated temperature (e.g., 83°).
IT 72956-09-3P, Carvedilol
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of carvedilol from 4-(oxirane-2-ylmethoxy)-9H-carbazole and 2-(2-methoxyphenoxy)ethylamine salts)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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L18 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412793 CAPLUS
DOCUMENT NUMBER: 140:395553
TITLE: Controlled release carvedilol compositions
INVENTOR(S): Andersen, Christine; Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Lademann, Anne-Marie
PATENT ASSIGNEE(S): Egalet A/S, Den.
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041252	A1	20040521	WO 2003-DK765	20031107
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003275953	A1	20040607	AU 2003-275953	20031107
US 2004151772	A1	20040805	US 2003-703084	20031107
EP 1562552	A1	20050817	EP 2003-810382	20031107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE, HU, SK				
CA 2520312	AA	20041007	CA 2004-2520312	20040326
WO 2004084869	A1	20041007	WO 2004-DK217	20040326
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1610768	A1	20060104	EP 2004-723523	20040326
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.:

DK 2002-1725	A	20021108
DK 2003-464	A	20030326
WO 2003-DK765	W	20031107
WO 2004-DK217	W	20040326

AB A controlled release pharmaceutical composition for oral use comprises carvedilol. The composition releases carvedilol after oral administration to a mammal, including a human, in such a manner that a prolonged residence of

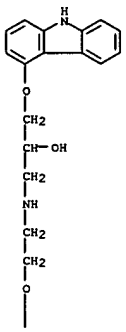
L18 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

carvedilol is obtained in the circulatory system compared with the known compns. of carvedilol. Furthermore, a compn. according to the present invention makes available to the body a suitable plasma concn. of one or both of the enantiomeric species, namely R(+) and/or S(-) carvedilol for obtaining the desired therapeutic effect. A matrix compn. contained PEG 64.6, carvedilol 30, and citric acid 5.4 mg. This matrix was coated to five and 50 mg. dosage form.

IT 72956-09-3, Carvedilol 95093-99-5, 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- 95094-00-1, S-Carvedilol
RL: PKT (Pharmacokinetics); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release carvedilol compns.)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

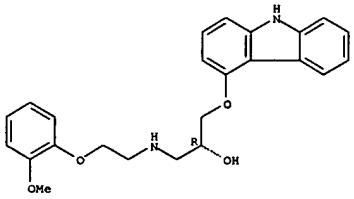


PAGE 2-A

RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

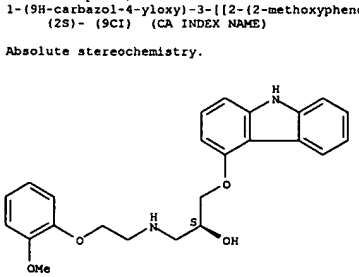
L18 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L18 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:20485 CAPLUS
DOCUMENT NUMBER: 140:82264
TITLE: Crystalline form of carvedilol hydrobromide for cardiovascular therapy
INVENTOR(S): Chen, Pingyun Y.; Dai, Qunying; Dell'orco, Phillip C.; Hisler, Claire; Igo, David H.; Katrincic, Lee M.; Labaw, Clifford S.; Ping, Li-jen
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002472	A1	20040108	WO 2003-US20346	20030627
WO 2004002472	C1	20050224		
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492084	AA	20040108	CA 2003-2492084	20030627
AU 2003251627	A1	20040119	AU 2003-251627	20030627
EP 1539140	A1	20050615	EP 2003-762148	20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005533822	T2	20051110	JP 2004-517980	20030627
US 2005261355	A1	20051124	US 2004-518206	20041216

PRIORITY APPLN. INFO.:

US 2002-392374P	P	20020627
WO 2003-US20346	W	20030627

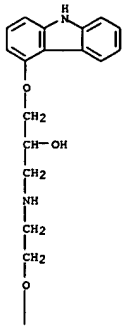
AB The present invention relates to a salt of carvedilol, corresponding compns. containing such a carvedilol salt or corresponding solvates thereof, and/or methods of using the aforementioned compound(s) in the treatment of certain disease states in mammals, in particular man. The present invention further relates to a novel crystalline form of carvedilol hydrobromide, which is the hydrobromide salt of 1-(carbazol-4-yloxy)-3-[[2-(methoxyphenoxy)ethyl]amino]-2-propanol, and/or other carvedilol solvates thereof, compns. containing salts or solvates of carvedilol hydrobromide, and methods of using the aforementioned compound(s) to treat hypertension, congestive heart failure, and angina, etc.

IT 374779-42-7DP, solvates 640724-11-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)

RN 374779-42-7 CAPLUS

L18 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



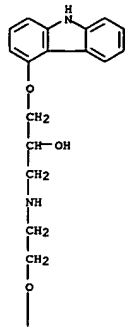
PAGE 2-A

● HBr

RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

L18 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

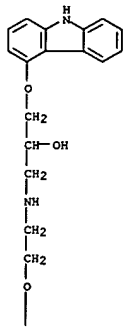
● HBr

● H_2O

IT 374779-42-7
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

L18 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HBr

IT 72956-09-3, Carvedilol
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrobromination and hydration; crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-
(9CI) (CA INDEX NAME)

L18 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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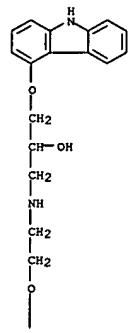

PAGE 2-A

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L18 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:20440 CAPLUS
DOCUMENT NUMBER: 140:71025
TITLE: Carvedilol phosphate salts and/or solvates thereof, corresponding compositions, and/or methods of treatment
INVENTOR(S): Brook, Christopher S.; Chen, Wei; Dell'orco, Philip C.; Katrincic, Lee M.; Louvet, Ann Marie; Oh, Choon K.; Spoors, Paul G.; Werner, Christopher
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002419	A2	20040108	WO 2003-US20408	20030627
WO 2004002419	A3	20040603		
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SC, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492060	AA	20040108	CA 2003-2492060	20030627
AU 2003248746	A1	20040119	AU 2003-248746	20030627
EP 1534270	A2	20050601	EP 2003-762176	20030627
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1678305	A	20051005	CN 2003-820230	20030627
JP 2005533823	T2	20051110	JP 2004-518025	20030627
US 2005240027	A1	20051027	US 2004-518654	20041216
NO 2005000427	A	20050125	NO 2005-427	20050125
PRIORITY APPLN. INFO.:			US 2002-392175P P	20020627
			WO 2003-US20408 W	20030627

AB The present invention relates to carvedilol phosphate salts, which include novel crystalline forms of carvedilol dihydrogen phosphate (i.e., dihydrogen phosphate salt of 1-(carbazol-4-yloxy-3-[[2-(o-methoxyphenoxy) ethyl]amino]-2-propanol) and/or carvedilol hydrogen phosphate, etc.), and/or solvates thereof, compns. containing the aforementioned salts and/or solvates, and methods of using the aforementioned salts and/or solvates to treat hypertension, congestive heart failure and angina, etc.

IT 374779-45-0 610309-89-2 641571-35-9
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol phosphate salts and/or solvates for treating hypertension, congestive heart failure and angina)

RN 374779-45-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L18 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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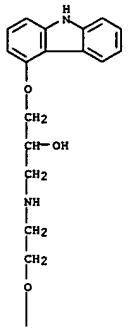

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CM 2

CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 610309-89-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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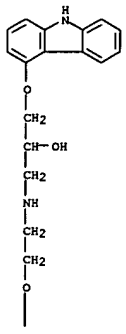

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CM 2

CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 641571-35-9 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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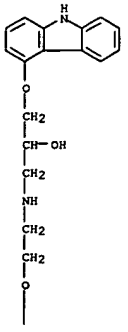

PAGE 2-A

CM 2

L18 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 7664-38-2
CMF H3 O4 P

L18 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:892566 CAPLUS
DOCUMENT NUMBER: 139:386333
TITLE: preparation of carvedilol monocitrate monohydrate for treatment of hypertension, congestive heart failure and angina
INVENTOR(S): Chen, Wei; Oh, Choon K.; Ping, Li-Jen J.; Spoors, Paul G.
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003092622	A2	20031113	WO 2003-US13832	20030430
WO 2003092622	A3	20040729		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2483054	AA	20031113	CA 2003-2483054	20030430
AU 2003231283	A1	20031117	AU 2003-231283	20030430
EP 1499310	A2	20050126	EP 2003-724421	20030430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005148779	A1	20050707	US 2003-512628	20030430
JP 2006500320	T2	20060105	JP 2004-500807	20030430
PRIORITY APPLN. INFO.:			US 2002-376599P	P 20020430
			US 2002-383287P	P 20020523
			WO 2003-US13832	W 20030430

AB This invention relates to preparation of carvedilol monocitrate monohydrate, compns. containing this salt of carvedilol and methods of using this compound to treat hypertension, congestive heart failure and angina. Crystalline carvedilol monocitrate monohydrate was prepared by making citric acid solution saturated with carvedilol and then crystallized from an acetone-water solvent system.

IT 623113-70-2P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline; preparation of carvedilol monocitrate monohydrate to treat hypertension and congestive heart failure and angina)
RN 623113-70-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L18 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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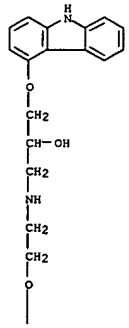

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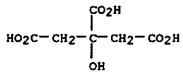
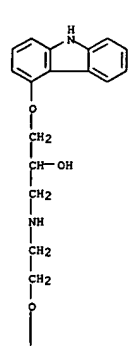
CRN 77-92-9
CMF C6 H8 O7

L18 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT 72956-09-3, Carvedilol
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of carvedilol monocitrate monohydrate to treat hypertension and congestive heart failure and angina)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L18 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:570906 CAPLUS
DOCUMENT NUMBER: 139:122716
TITLE: Crystalline solids of carvedilol and processes for their preparation
INVENTOR(S): Kor, Ilan; Wizel, Shlomit
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059807	A2	20030724	WO 2003-US1137	20030115
WO 2003059807	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472377	AA	20030724	CA 2003-2472377	20030115
AU 2003205146	A1	20030730	AU 2003-205146	20030115
US 2003166702	A1	20030904	US 2003-342905	20030115
US 6710184	B2	20040323		
EP 1474133	A2	20041110	EP 2003-703815	20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1615133	A	20050511	CN 2003-802210	20030115
JP 2005515226	T2	20050526	JP 2003-559922	20030115
US 2004171665	A1	20040902	US 2003-712799	20031112
ZA 2004005443	A	20050708	ZA 2004-5443	20040708
NO 2004003383	A	20040813	NO 2004-3383	20040813

PRIORITY APPLN. INFO.:
US 2002-349310P P 20020115
US 2003-342905 A3 20030115
WO 2003-US1137 W 20030115

AB This invention relates to a novel crystalline solid of carvedilol or a solvate thereof, to processes for its preparation, to compns. containing it and to its use in medicine. This invention further relates to a novel process for preparing a crystalline solid of carvedilol form II.

IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline solids of carvedilol and processes for their preparation)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L18 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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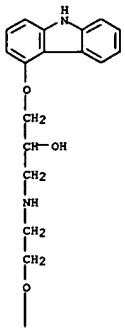

PAGE 2-A

L18 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:282536 CAPLUS
DOCUMENT NUMBER: 138:292802
TITLE: Pseudopolymorphic forms of carvedilol
INVENTOR(S): Bubendorf, Andre Gerard; Gabel, Rolf-dieter; Henning, Michael; Krimmer, Siegfried; Neugebauer, Guenter; Preis, Walter; Wirl, Alexander
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029214	A1	20030410	WO 2002-EP10451	20020918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2460486	AA	20030410	CA 2002-2460486	20020918
EP 1432681	A1	20040630	EP 2002-777139	20020918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012927	A	20041013	BR 2002-12927	20020918
CN 1558900	A	20041229	CN 2002-818741	20020918
JP 2005507899	T2	20050324	JP 2003-532464	20020918
US 2003119893	A1	20030626	US 2002-255290	20020926
US 2004198812	A1	20041007	US 2004-827859	20040420
US 2006148878	A1	20060706	US 2006-325754	20060105

PRIORITY APPLN. INFO.:
EP 2001-123422 A 20010928
WO 2002-EP10451 W 20020918
US 2002-255290 B1 20020926
US 2004-827859 B1 20040420

AB The present invention is related to pseudopolymorphic forms of 1-(4-carbazolyloxy)-3[2-(2-methoxyphenoxy)ethylamino]-2-propanol (carvedilol) or its optically active forms or pharmaceutically acceptable salts, processes for their preparation, and pharmaceutical compns. containing them for the treatment or prophylaxis of cardiac diseases.

IT 507239-85-2
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pseudopolymorphic forms of carvedilol for modified-release dosage forms for treatment of cardiac diseases)
RN 507239-85-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L18 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
hydrate (2:1) (9CI) (CA INDEX NAME)

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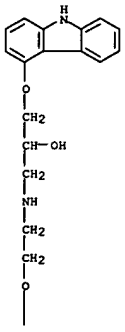

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●1/2 H_2O

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pseudopolymorphic forms of carvedilol for modified-release dosage forms for treatment of cardiac diseases)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L18 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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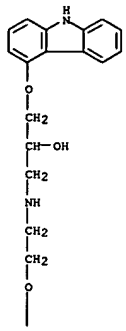

PAGE 2-A

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L18 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

water soly. are also disclosed. Thus, a compn. contained PEG 64.6, carvedilol 30, and citric acid 5.4% by wt.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)

RN 72956-09-3 CAPLUS

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

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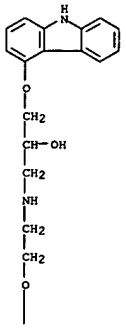

PAGE 2-A

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L18 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:242149 CAPLUS
DOCUMENT NUMBER: 138:276256
TITLE: Controlled release pharmaceutical compositions containing polymers
INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Lademann, Anne-Marie; Jensen, Christine
PATENT ASSIGNEE(S): Egalet A/S, Den.
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024429	A1	20030327	WO 2002-DK620	20020923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429739	A1	20040623	EP 2002-779224	20020923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004234602	A1	20041125	US 2004-490308	20040623
PRIORITY APPLN. INFO.:			DK 2001-1377	A 20010921
			DK 2002-1044	A 20020703
			WO 2002-DK620	W 20020923

AB A method for controlling the release of at least one therapeutically, prophylactically and/or diagnostically active substance into an aqueous medium by erosion of at least one surface of a pharmaceutical composition The method comprises adjusting the concentration and/or the nature of the ingredients making up the matrix composition in such a manner so as to obtain an approx. zero-order release of the drug from the pharmaceutical composition when subject to an in vitro dissoln. test as described herein. The composition comprises a matrix composition containing a polymer or a mixture of polymers that may be substantially water soluble and/or crystalline, an active substance and, optionally, one or more pharmaceutically acceptable excipients, and a coating. Typical polymers are PEG. The coating comprises a first cellulose derivative which is substantially insol. in the aqueous medium, and at least one of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and a filler. The active ingredient may be carvedilol. Stable solid dispersions of active substances having low

L18 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:242148 CAPLUS
DOCUMENT NUMBER: 138:276255
TITLE: Controlled release solid dispersions containing carvedilol
INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Lademann, Anne-Marie; Jensen, Christine
PATENT ASSIGNEE(S): Egalet A/S, Den.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024426	A1	20030327	WO 2002-DK621	20020923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429734	A1	20040623	EP 2002-776907	20020923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005019399	A1	20050127	US 2004-490170	20040921
PRIORITY APPLN. INFO.:			DK 2001-1375	A 20010921
			DK 2001-1611	A 20011031
			DK 2002-1044	A 20020703
			WO 2002-DK621	W 20020923

AB A controlled release pharmaceutical composition for oral use comprises a solid dispersion of at least one therapeutical agent and/or diagnostic substance, which at least partially is in an amorphous form, a polymer that has plasticizing properties, and optionally, a stabilizing agent, the at least one active substance having a limited water solubility, and the composition being designed to release the active substance with a substantially zero order release. The polymer is typically a polyethylene glycol and/or polyethylene oxide having a mol. weight of at least about 20,000 in crystalline and/or amorphous form or a mixture of such polymers, and the active substance is typically carvedilol. The composition may comprise a coated matrix, the coating comprising a first cellulose derivative which is substantially insol. in the aqueous medium, and at least one of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and a filler. Thus, a composition contained PEG 64.6, carvedilol 30, and citric acid 5.4% by weight The dissoln. profile corresponded to a zero-order

L18 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
release of carvedilol from the compn.
IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release solid dispersions containing carvedilol)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

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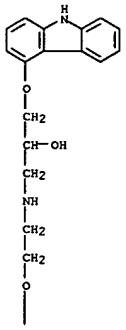

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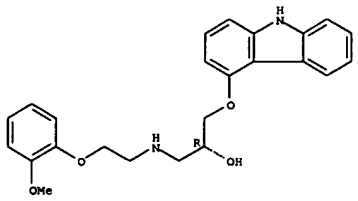
IT 95093-99-5 95094-00-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release solid dispersions containing carvedilol)
RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

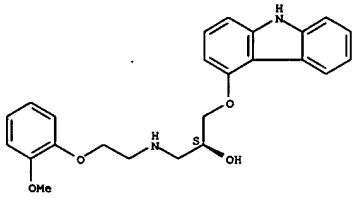
Absolute stereochemistry.

L18 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:57865 CAPLUS
DOCUMENT NUMBER: 138:126962
TITLE: Carvedilol polymorph
INVENTOR(S): Chen, Wei; Gallop, Marc; Oh, Choon K.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003005970	A2	20030123	WO 2002-US22374		20020715
WO 2003005970	A3	20030501			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1406614	A2	20040414	EP 2002-761099		20020715
EP 1406614	B1	20060607			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2004534840	T2	20041118	JP 2003-511779		20020715
AT 328595	E	20060615	AT 2002-761099		20020715
US 2004152756	A1	20040805	US 2004-483217		20040108
PRIORITY APPLN. INFO.:			US 2001-305593P	P	20010713
			US 2001-314150P	P	20010822
			WO 2002-US22374	W	20020715

AB This invention relates to a crystalline form of carvedilol (Form III), and to the use of pharmaceutical compns. containing carvedilol Form III for treatment of hypertension, angina, or congestive heart failure. The carvedilol Form III was prepared from carvedilol Form II.
IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and properties of carvedilol polymorph)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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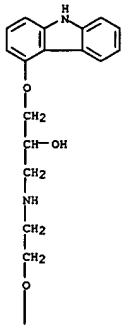

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L18 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:754995 CAPLUS
DOCUMENT NUMBER: 137:268473
TITLE: Porous drug matrices and methods of manufacture thereof
INVENTOR(S): Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002142050	A1	20021003	US 2002-53929	20020122
US 6395300	B1	20020528	US 1999-433486	19991104
EP 1642572	A1	20060405	EP 2005-27194	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 6645528	B1	20031111	US 2000-694407	20001023
US 6932983	B1	20050823	US 2000-706045	20001103
ZA 2001010347	A	20030730	ZA 2001-10347	20011218
US 2005048116	A1	20050303	US 2004-924642	20040824
US 2005058710	A1	20050317	US 2004-928886	20040827
PRIORITY APPLN. INFO.:			US 1999-136323P	P 19990527
			US 1999-158659P	P 19991008
			US 1999-433486	A2 19991104
			US 2000-186310P	P 20000302
			EP 2000-939365	A3 20000525
			US 2002-53929	A3 20020122

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in crystalline form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln.

L18 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aq. medium and administered parenterally, or processed using std. techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A soln. of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the org. soln. (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.
IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

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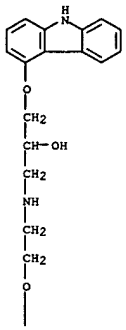

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L18 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:107159 CAPLUS
DOCUMENT NUMBER: 136:172753
TITLE: Epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure
INVENTOR(S): Alexander, John C.; Schuh, Joseph R.
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009760	A2	20020207	WO 2001-US23670	20010727
WO 2002009760	A3	20030123		
WO 2002009760	C2	20030904		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2415789	AA	20020207	CA 2001-2415789	20010727
AU 2001079050	A5	20020213	AU 2001-79050	20010727
US 2002123485	A1	20020905	US 2001-917403	20010727
EP 1303306	A2	20030423	EP 2001-957290	20010727
EP 1303306	B1	20060621		
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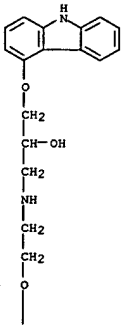
JP 2004511435	T2	20040415	JP 2002-515312	20010727
AT 330633	E	20060715	AT 2001-957290	20010727
US 2004235809	A1	20041125	US 2004-343166	20040607
US 2005215537	A1	20050929	US 2005-143310	20050602
PRIORITY APPLN. INFO.:			US 2000-221365P	P 20000727
			US 2001-917403	A1 20010727
			WO 2001-US23670	W 20010727

AB A combination therapy comprising a therapeutically-effective amount of an epoxy-steroidal aldosterone receptor antagonist and a therapeutically-effective amount of a beta-adrenergic antagonist is described for treatment of circulatory disorders, including cardiovascular disorders such as hypertension, congestive heart failure, cirrhosis and ascites. Preferred beta-adrenergic antagonists are those compds. having high potency and bioavailability. Preferred epoxy-steroidal aldosterone receptor antagonists are 20-spiroxane steroidal compds. characterized by the presence of a 9α, 11α-substituted epoxy moiety. A preferred combination therapy includes the beta-adrenergic antagonist metoprolol succinate and the aldosterone receptor antagonist epoxymexrenone. Crystal forms of eplerenone were prepared as well as the Me Et ketone solvate.

L18 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(epoxy-steroidal aldosterone antagonist and beta-adrenergic antagonist combination therapy for treatment of congestive heart failure)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

L18 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:10275 CAPLUS
DOCUMENT NUMBER: 136:90914
TITLE: Preparation of carvedilol and its crystalline hydrate and solvate
INVENTOR(S): Hildesheim, Jean; Finogueev, Sergey; Aronhime, Judith; Dolitzky, Ben-Zion; Ben-Valid, Shoshana; Kor, Ilan
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000216	A1	20020103	WO 2001-US20760	20010628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413702	AA	20020103	CA 2001-2413702	20010628
US 2002143045	A1	20021003	US 2001-894798	20010628
US 6699997	B2	20040302		
EP 1299101	A1	20030409	EP 2001-950671	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501191	T2	20040115	JP 2002-504998	20010628
CN 1733727	A	20060215	CN 2005-10086095	20010628
EP 1655285	A1	20060510	EP 2005-21195	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 2002010282	A	20031219	ZA 2002-10282	20021219
US 2004152757	A1	20040805	US 2004-758025	20040116
US 7056942	B2	20060606		
US 2004225132	A1	20041111	US 2004-758026	20040116
US 2006030614	A1	20060209	US 2005-217643	20050831

PRIORITY APPLN. INFO.:

US 2000-214356P	P	20000628
US 2000-246358P	P	20001107
CN 2001-814616	A3	20010628
EP 2001-950671	A3	20010628
US 2001-894798	A3	20010628
WO 2001-US20760	W	20010628
US 2004-758025	A3	20040116

AB This invention relates to an improved process of preparing carvedilol, as well as a new crystalline hydrate and solvate and forms of

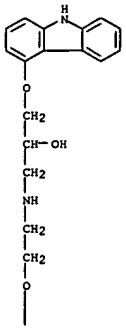
L18 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

carvedilol, processes for the manuf. thereof, and pharmaceutical compns. thereof. Carvedilol was prepd. by the reaction of 2-(2-methoxyphenoxy)ethylamine and 4-(oxiran-2-ylmethoxy)-9H-carbazole. Cryst. carvedilol form II was prepd. by crystg. carvedilol from isoamyl alc.

IT 72956-09-3P, Carvedilol 385765-36-6P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carvedilol and its crystalline hydrate and solvate)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A

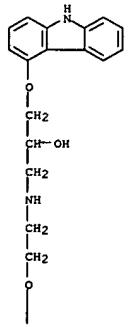


PAGE 2-A

RN 385765-36-6 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, hydrochloride, hydrate (9CI) (CA INDEX NAME)

L18 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

●x HCl

●x H_2O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L18 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:

US 1999-165398P	P	19991105
US 2000-196571P	P	20000411

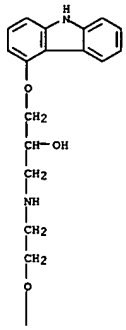
AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 72956-09-3 CAPLUS

L18 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A

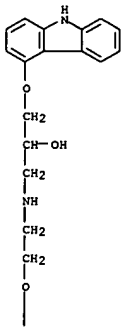


PAGE 2-A

L18 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:312052 CAPLUS
DOCUMENT NUMBER: 135:127050
TITLE: Detection of low levels of the amorphous phase in crystalline pharmaceutical materials by thermally stimulated current spectrometry
AUTHOR(S): Venkatesh, Gopi M.; Barnett, Maria E.; Owusu-Fordjour, Charles; Galop, Marc
CORPORATE SOURCE: SB Pharmaceutical, Collegeville, PA, 19426, USA
SOURCE: Pharmaceutical Research (2001), 18(1), 98-103
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose. To demonstrate the applicability of thermally stimulated current (TSC) spectrometry for the detection of low levels of the amorphous phase in crystalline pharmaceutical materials. Methods. A crystalline drug substance was melt quenched to produce an amorphous material. Blends of the crystalline and amorphous phases in different ratios (from 75:25 to 99:01) were prepared by serial dilution TSC studies were performed by applying an elec. field at a temperature above the glass transition temperature (Tg) to orient the dipoles, rapidly cooling to 0°, short circuiting for 1 min. and scanning at 7°/min to measure the depolarization current. The temperature of the peak in the spectrum corresponds to the Tg of the amorphous phase. Modulated DSC studies were performed by using 3 different test protocols (varying linear heating rate, modulation amplitude, and time period). Powder x-ray diffraction (XRD) studies were performed. Results. The ability to detect the amorphous phase by powder XRD is beset with problems due to indirect inference, orientation effects, and instrument-related intensity variations. Even using a consistent sampling procedure and an internal standard, the XRD could quantify the amorphous phase at a level of 5%. In the conventional or modulated DSC, the amorphous phase manifests itself as a shift in the baseline. Using modulated DSC it was possible to detect the amorphous phase at a level of 5% when tested at a heating rate of 2°/min and an amplitude of 1.0° with a period of 30 s. The moisture sorption method appears to have a similar detection capability. In TSC scans, the glass transition event due to mol./segmental mobility in the amorphous phase was manifested as a peak/shoulder on the low-temperature side of the depolarization peak of the crystalline phase. The amorphous phase was unambiguously detected at 2% with a lower detection limit of 1%. Conclusions. On the basis of the results of this preliminary investigation. TSC appears to be capable of detecting the amorphous phase at as low as 1% in cryst . pharmaceuticals, thus offering a much needed capability in discerning factors.
IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of low levels of amorphous phase in crystalline pharmaceuticals by thermally stimulated current spectrometry)
RN 72956-09-3 CAPLUS

L18 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:96212 CAPLUS
DOCUMENT NUMBER: 130:158418
TITLE: Thermodynamically stable modification of 1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-2-propanol, process for its preparation and pharmaceutical compositions containing it
INVENTOR(S): Reinholz, Erhard; Beyer, Peter
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

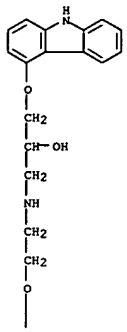
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9905105	A1	19990204	WO 1998-EP4475	19980718
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 893440	A1	19990127	EP 1997-112491	19970722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2296637	AA	19990204	CA 1998-2296637	19980718
CA 2296637	C	20051115		
AU 9886319	A1	19990216	AU 1998-86319	19980718
AU 740453	B2	20011101		
EP 1000027	A1	20000517	EP 1998-937576	19980718
EP 1000027	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9810776	A	20000919	BR 1998-10776	19980718
JP 2001510824	T2	20010807	JP 2000-504104	19980718
NZ 502136	A	20020531	NZ 1998-502136	19980718
AT 236123	E	20030415	AT 1998-937576	19980718
RU 2202542	C2	20030420	RU 2000-103033	19980718
IL 133677	A1	20040601	IL 1998-133677	19980718
PL 191602	B1	20060630	PL 1998-338432	19980718
MX 200000507	A	20001109	MX 2000-507	20000113
NO 2000000301	A	20000121	NO 2000-301	20000121
NO 313588	B1	20021028		
HK 1029339	A1	20040213	HK 2001-100012	20010102
US 2003036559	A1	20030220	US 2002-166188	20020610
US 6730326	B2	20040504		

PRIORITY APPLN. INFO.: EP 1997-112491 A 19970722
WO 1998-EP4475 W 19980718
US 2000-463346 B1 20000121

AB The present invention relates to a new thermodynamically stable modification of Carvedilol, pharmacol. acceptable salts, or optically active forms thereof, processes for the preparation, and pharmaceutical compns.

L18 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
contg. it. Crude carvedilol is heated with MeOH and CXA-coal to give forms I and II and these are recrystd. in isopropanol to give pure form I.
IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(crystal modification of carvedilol for pharmaceuticals)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

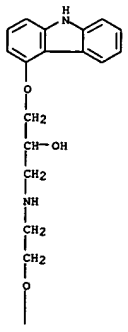
L18 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:90419 CAPLUS
DOCUMENT NUMBER: 130:144175
TITLE: Thermodynamically stable modification of carvedilol, process for its preparation and pharmaceutical compositions containing it
INVENTOR(S): Beyer, Peter; Reinholz, Erhard
PATENT ASSIGNEE(S): Boehringer Mannheim GmbH, Germany
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 893440	A1	19990127	EP 1997-112491	19970722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CA 2296637	AA	19990204	CA 1998-2296637	19980718
CA 2296637	C	20051115		
WO 9905105	A1	19990204	WO 1998-EP4475	19980718
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886319	A1	19990216	AU 1998-86319	19980718
AU 740453	B2	20011101		
EP 1000027	A1	20000517	EP 1998-937576	19980718
EP 1000027	B1	20030402		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200000148	T2	20000721	TR 2000-200000148	19980718
BR 9810776	A	20000919	BR 1998-10776	19980718
JP 2001510824	T2	20010807	JP 2000-504104	19980718
NZ 502136	A	20020531	NZ 1998-502136	19980718
TW 505631	B	20021011	TW 1998-87111738	19980718
AT 236123	E	20030415	AT 1998-937576	19980718
RU 2202542	C2	20030420	RU 2000-103033	19980718
PT 1000027	T	20030731	PT 1998-937576	19980718
CN 1125047	B	20031022	CN 1998-807436	19980718
ES 2195366	T3	20031201	ES 1998-937576	19980718
IL 133677	A1	20040601	IL 1998-133677	19980718
PL 191602	B1	20060630	PL 1998-338432	19980718
ZA 9806475	A	20000121	ZA 1998-6475	19980721
MX 200000507	A	20001109	MX 2000-507	20000113
NO 2000000301	A	20000121	NO 2000-301	20000121
NO 313588	B1	20021028		
HK 1029339	A1	20040213	HK 2001-100012	20010102
US 2003036559	A1	20030220	US 2002-166188	20020610
US 6730326	B2	20040504		

PRIORITY APPLN. INFO.: EP 1997-112491 A 19970722
WO 1998-EP4475 W 19980718
US 2000-463346 B1 20000121

L18 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
AB A new thermodynamically stable modification of 1-(4-carbazolyloxy)-3-[2-(2-methoxyphenoxy)ethylamino]-2-propanol (carvedilol), pharmacol. acceptable salts, or optically active forms thereof, processes for the preparation, and pharmaceutical compns. containing it is disclosed. Thus, 300 g crude carvedilol, 15 g CXA-coal and 2800 methanol was heated for 15 min under reflux, then the hot solution was filtered, washed with 300 mL hot methanol and heated under reflux again. Subsequently the solution was cooled down to 0° and the product was isolated, washed with methanol and dried to obtain 203-255 g of pure form I. Form II can be obtained by addnl. recrystn. process in isopropanol.
IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(thermodynamically stable modification of carvedilol, process for its preparation and pharmaceutical compns. containing it)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



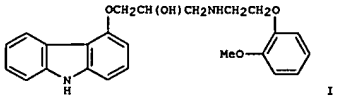
L18 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:654214 CAPLUS
DOCUMENT NUMBER: 130:3743
TITLE: Synthesis and crystal structure of carvedilol
AUTHOR(S): Chen, Wei-Min; Zeng, Long-Mei; Yu, Kai-Bei; Xu, Ji-Hong
CORPORATE SOURCE: Inst. Pharmaceutical Sci., The First Military Med. Univ., Canton, 510515, Peop. Rep. China
SOURCE: Jiegou Huaxue (1998), 17(5), 325-328
CODEN: JHUADF; ISSN: 0254-5861
PUBLISHER: "Jiegou Huaxue" Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The crystal structure of carvedilol (I), prepared from 4-(2,3-epoxypropoxy)carbazole and 2-MeOC6H4OCH2CH2NH2, was determined by single-crystal x-ray diffraction. The crystal is composed of a pair of enantiomers, and there are hydrogen bonds O-H-N between the two enantiomers. There are two planes in the mol.

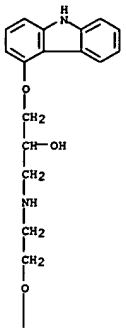
IT 72956-09-3P, Carvedilol
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)

RN 72956-09-3 CAPLUS

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:551608 CAPLUS
DOCUMENT NUMBER: 125:268661
TITLE: Carvedilol-liposome interaction: evidence for strong association with the hydrophobic region of the lipid bilayers
AUTHOR(S): Cheng, Hung-Yuan; Randall, Cynthia S.; Holl, Walter W.; Constantinides, Panayiotis P.; Yue, Tian-Li; Feuerstein, Giora Z.
CORPORATE SOURCE: Physical and Structural Chemistry, SmithKline Beecham Pharmaceuticals, 709 Swedeland Road, King of Prussia, USA
SOURCE: Biochimica et Biophysica Acta, Biomembranes (1996), 1284(1), 20-28
CODEN: BBBMBS; ISSN: 0005-2736
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carvedilol (Kredex, Coreg) is a multiple action antihypertensive drug that has been shown to protect cell membranes from lipid peroxidative damages. In this study the phys. and structural effects of carvedilol on lipid bilayers are investigated by fluorescence techniques, differential scanning calorimetry and other phys. methods. Carvedilol binds to liposomal membranes (9:1 DMPC:DMPG) strongly with an apparent binding constant on the order of 104 M-1 in PBS (pH 7.4). The characteristic changes in its intrinsic fluorescence properties when bound to liposomes suggest that this compound is situated in a non-polar environment. The Stern-Volmer and bimol. quenching consts., determined using nitrate as the fluorescence quencher, for the free and bound carvedilol indicate that the carbazole moiety is at a depth of >11 Å in the lipid bilayer. Fluorescence anisotropy measurements show that, unlike the membrane probes DPH and TMA-DPH, carvedilol is relatively mobile, and does not have a rigidly-defined mol. orientation in the bilayers. Differential scanning calorimetry results indicate that carvedilol is an effective membrane 'fluidizer' as it dose-dependently lowers the gel to liquid crystalline transition temperature and broadens the endothermic transition. Comparative studies of interactions of carbazole, 4-OH carbazole and carvedilol with the model liposomal membranes reveal a possible role of membrane-partitioning in their antioxidant efficacy. These findings are discussed in perspective with the membrane biophys. properties of different classes of therapeutic significant lipid antioxidants in mind.

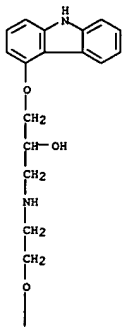
IT 72956-09-3, Carvedilol
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(carvedilol-liposome interaction: evidence for strong association with the hydrophobic region of the lipid bilayers)

RN 72956-09-3 CAPLUS

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L18 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

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L22 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:367270 CAPLUS
DOCUMENT NUMBER: 144:398367
TITLE: Amorphous pharmaceutical compositions comprising rosiglitazone
INVENTOR(S): Ignatious, Francis; Sun, Linghong; Craig, Andrew; Crowe, David; Ho, Tim; Millan, Michael
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 523,835.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006083784	A1	20060420	US 2005-64890	20050224
WO 2004014304	A2	20040219	WO 2003-US24641	20030807
WO 2004014304	A3	20040624		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006013869	A1	20060119	US 2005-523835	20050207

PRIORITY APPLN. INFO.: US 2002-401726P P 20020807
WO 2003-US24641 W 20030807
US 2005-523835 A2 20050207

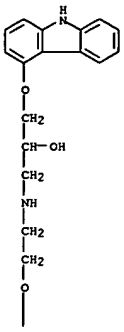
AB The present invention is directed to use of electrospinning, i.e. the process of making polymer nanofibers from either a solution or melt under elec. forces, to prepare stable, solid dispersions of amorphous drugs in polymer nanofibers. The present invention is also directed to the process of making solid dispersions of amorphous forms and compns. of rosiglitazone and its pharmaceutically acceptable salts. A 3.1 weight% solution of rosiglitazone mesylate 2-PrOH-water was spray dried to give an amorphous powder.

IT 640724-11-4
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amorphous pharmaceutical compns. comprising rosiglitazone)

RN 640724-11-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

L22 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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● HBr

● H_2O

L22 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:694938 CAPLUS
DOCUMENT NUMBER: 143:482873
TITLE: Paediatric formulations-Getting to the heart of the problem
AUTHOR(S): Standing, Joseph F.; Tuleu, Catherine
CORPORATE SOURCE: Pharmacy Department, Great Ormond Street Hospital for Children NHS Trust, London, WC1N 3JH, UK
SOURCE: International Journal of Pharmaceutics (2005), 300(1-2), 56-66
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

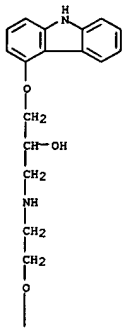
AB Many medicines prescribed for children are unlicensed. Solid dosage forms present problems as children have difficulty swallowing whole tablets or capsules. When medicines are not licensed for children, it is unlikely that there will be a suitable, licensed liquid formulation and so extemporaneous liquid prepns. (prepared at the dispensary or by GMP 'special' manufacturers) are often used. This study looked at a list of medicines commonly prescribed for children with cardiovascular conditions in an English specialist pediatric hospital and classified them according to licensed status and available formulations. As expected, most medicines used for children with cardiovascular problems were unlicensed and where this was the case, usually only 'special' liqs. or extemporaneous prepns. were available. Problems linked with formulations highlighted in this therapeutic category were: problems in dosing accuracy and unknown bioavailability of extemporaneous products, the use of potentially toxic excipients, and lack of access to modified release prepns. for children. These problems are likely to extend to other pediatric therapeutic areas. There is currently a large, unmet need to improve formulations of commonly used pediatric medicines, both through licensing and standardizing the production of extemporaneous and 'special' formulations. It is expected that the awaited European regulation will help to meet some of those needs.

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pediatric formulations for cardiovascular drugs)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L22 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:490267 CAPLUS
DOCUMENT NUMBER: 141:42919
TITLE: Free-flowing solid formulations with improved bio-availability of poorly water soluble drugs and process for making the same
INVENTOR(S): Li, Wenji; Alosio, Edward; Dema-Ala, Bricini Faith; Nguyen, Amy
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004115226	A1	20040617	US 2002-317657	20021212
WO 2004054540	A2	20040701	WO 2003-US38979	20031209
WO 2004054540	A3	20040930		

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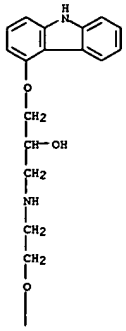
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2003300833	A1	20040709	AU 2003-300833	20031209
JP 2006511536	T2	20060406	JP 2004-560372	20031209
PRIORITY APPLN. INFO.:			US 2002-317657	A 20021212
			WO 2003-US38979	W 20031209

AB Disclosed is a free-flowing solid formulations of drugs or pharmaceutical agents which have poor aqueous solubility are obtained by admixing a liquid or gel composition that includes 1-30 % of the drug, 5-60 % of a surfactant, 10-40 % of water; 1-20 % of unsatd. fatty acid ester, 0-50 % water miscible pharmaceutically acceptable polyol and 1-10 % phospholipid with a pharmaceutically acceptable suitable solid carrier and thereafter drying the admixt. The free-flowing powder is suitable for being formed into tablets or capsules. The drug or pharmaceutical agent is solubilized in the formulation and has significantly improved bio-availability when compared to the drug tested in its pure form . A gel composition containing polyoxyethylene sorbitan monooleate 35, propylene glycol 25, Et linoleate 8, simvastatin 4, and 5 % lecithin aqueous solution q.s. to 100 % was formulated. Colloidal silicon dioxide 30 parts was granulated with the obtained gel 70 parts. The granules was dried to provide a free-flowing powder. When this powder was exposed to a gastric medium of pH 1.2, 67 % of the drug simvastatin dissolved within 10 min.
IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(free-flowing solid formulations with improved bio-availability of poorly water soluble drugs obtained from gel compns.

L22 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
contg. surfactants, fatty acid esters, polyols, and phospholipids)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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L22 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:862712 CAPLUS
DOCUMENT NUMBER: 140:133838
TITLE: Carvedilol-based solid medicinal form
PATENT ASSIGNEE(S): Otkrytoe Aktsionernoe Obshchestvo "Khimiko-Farmatsevticheskii Kombinat "Akrikhin", Russia
SOURCE: Russ., No pp. given
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2214243	C2	20031020	RU 2001-132735	20011205
PRIORITY APPLN. INFO.:			RU 2001-132735	20011205

AB The invention relates to a solid medicinal form of carvedilol made as a solid medicinal form containing carvedilol and pharmaceutically acceptable accessory substance among them starch, stearic acid and/or its salt are used.
IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(carvedilol-based solid medicinal form)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

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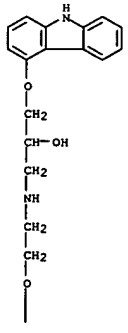

L22 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

L22 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:747606 CAPLUS
DOCUMENT NUMBER: 135:293976
TITLE: Hydrophilic molecular disperse solutions of carvedilol
INVENTOR(S): Gabel, Rolf-dieter; Wirl, Alexander; Preis, Walter; Neugebauer, Guenter
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074357	A1	20011011	WO 2001-EP3502	20010328
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001036959	A1	20011101	US 2001-817308	20010326
CA 2401910	AA	20011011	CA 2001-2401910	20010328
EP 1272179	A1	20030108	EP 2001-929462	20010328
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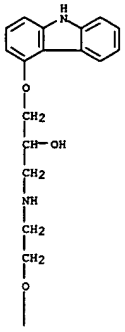
BR 2001009779	A	20030121	BR 2001-9779	20010328
JP 2003528915	T2	20030930	JP 2001-572101	20010328
NZ 521232	A	20040528	NZ 2001-521232	20010328
RU 2248204	C2	20050320	RU 2002-129571	20010328
US 2003004205	A1	20030102	US 2002-214697	20020808
ZA 2002007304	A	20031211	ZA 2002-7304	20020911
NO 2002004733	A	20021002	NO 2002-4733	20021002
US 2005271721	A1	20051208	US 2005-204614	20050816

PRIORITY APPLN. INFO.:		
EP 2000-107093	A	20000403
US 2001-817308	A1	20010326
WO 2001-EP3502	W	20010328
US 2002-214697	A1	20020808

AB The present invention is concerned with pharmaceutically acceptable compns. comprising carvedilol or a pharmaceutically acceptable salt thereof distributed as a mol. dispersion in a concentration above 5% (weight/weight), as well as pharmaceutical administration forms comprising such compns. and their use for the treatment and/or prophylaxis of illnesses such as hypertension, cardiac insufficiency or angina pectoris. Thus, 250.0 g of polyethylene glycol 6,000 was melted at 70° and mixed with 50.0 g of carvedilol and homogeneously dissolved. The melt was then spray solidified to the carvedilol solid solution
IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hydrophilic mol. disperse solns. of carvedilol)
RN 72956-09-3 CAPLUS

L22 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:861473 CAPLUS
DOCUMENT NUMBER: 134:32972
TITLE: Porous drug matrixes containing polymers and sugars and methods of their manufacture
INVENTOR(S): Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072827	A2	20001207	WO 2000-US14578	20000525
WO 2000072827	A3	20010125		
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US 6395300	B1	20020528	US 1999-433486	19991104
CA 2371836	AA	20001207	CA 2000-2371836	20000525
CA 2371836	C	20060131		
EP 1180020	A2	20020220	EP 2000-939365	20000525
EP 1180020	B1	20051214		
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BR 2000010984	A	20020430	BR 2000-10984	20000525
JP 2003500438	T2	20030107	JP 2000-620939	20000525
NZ 516083	A	20030829	NZ 2000-516083	20000525
AU 768022	B2	20031127	AU 2000-54459	20000525
AT 312601	E	20051215	AT 2000-939365	20000525
EP 1642572	A1	20060405	EP 2005-27194	20000525
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US 2002041896	A1	20020411	US 2001-798824	20010302
US 6610317	B2	20030826		
NO 2001005753	A	20020128	NO 2001-5753	20011126
ZA 2001010347	A	20030730	ZA 2001-10347	20011218

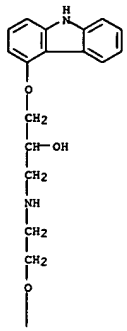
PRIORITY APPLN. INFO.:		
US 1999-136323P	P	19990527
US 1999-158659P	P	19991008
US 1999-433486	A	19991104
US 2000-186310P	P	20000302
EP 2000-939365	A3	20000525
WO 2000-US14578	W	20000525

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix

L22 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
form, preferably microparticles, which enhances dissoln. of the drug in aq. media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aq. soly., in a volatile solvent to form a drug soln., (ii) combining at least one pore forming agent with the drug soln. to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second soln. to yield the porous matrix of drug. The pore forming agent can be either a volatile liq. that is immiscible with the drug solvent or a volatile solid compd., preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aq. medium and administered parenterally, or processed using std. techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded org. soln. was prepd. by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aq. soln. was prepd. by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aq. and org. solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepd. in 5% dextrose soln. at a concn. of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.
IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L22 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

L22 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:383901 CAPLUS
DOCUMENT NUMBER: 133:22442
TITLE: Pharmaceutical combination preparations for treatment of cardiac and cardiovascular disorders
INVENTOR(S): Heller, Rudolf
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032174	A2	20000608	WO 1999-EP8972	19991120
WO 2000032174	A3	20001116		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
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TR 200101470	T2	20011121	TR 2001-200101470	19991120
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JP 2002531395	T2	20020924	JP 2000-584870	19991120
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PT 1131072	T	20030829	PT 1999-957320	19991120
AU 765977	B2	20031009	AU 2000-15065	19991120
ES 2195638	T3	20031201	ES 1999-957320	19991120
US 6403579	B1	20020611	US 1999-447872	19991123
TW 228414	B1	20050301	TW 2000-89103144	20000223
ZA 2001004280	A	20020826	ZA 2001-4280	20010524
US 2002052367	A1	20020502	US 2001-946205	20010905
US 2004087578	A1	20040506	US 2003-693243	20031024

PRIORITY APPLN. INFO.:

EP 1998-122489	A	19981127
WO 1999-EP8972	W	19991120
US 1999-447872	A3	19991123
US 2001-946205	B1	20010905

AB Pharmaceutical prepns. for the treatment of cardiac and cardiovascular disorders such as hypertension, angina pectoris, cardiac insufficiency, and illnesses associated therewith contain carvedilol, a β-blocker with addnl. α1-blocking activity, or a salt thereof and hydrochlorothiazide, a diuretic, or a salt thereof as a fixed combination of active substances, as well as usual additives. The process for production of the combination preparation permits the 2 active substance granulates to be

L22 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

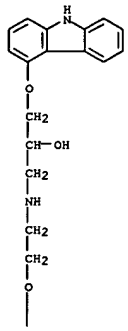
pressed to a stable tablet in 1 operation, as follows: granulates of the 2 agents, each having a moisture content of 6-20% and a bulk d. of 0.1-1.5 g/mL, and the granulate moisture content and bulk d. of the 2 granulates differing from one another by ≤30%. are combined to a press mass which is compressed to a solid dosage form, preferably a tablet. Since carvedilol is light sensitive, the dosage form is coated with a light-protecting film. At disintegrant contents >5%, the coating is applied at an initial spray rate sufficiently low to permit formation of a film on the tablet surface under conditions of air supply and temp. which remove the water of the film suspension as rapidly as possible from the tablet surface; after this crit. phase of film formation is complete, the spray rate is increased to that conventional for film-coating. Thus, tablets were prepd. contg. carvedilol 25.000, hydrochlorothiazide 12.500, sucrose 25.000, lactose-H2O 28.060, PVP 1.780, crosslinked PVP 20.170, microcryst. cellulose 10.000, highly dispersed SiO2 5.320, and Mg stearate 2.170 mg, and coated with a mixt. of Et acrylate/Me acrylate copolymer 2.248, Na citrate 0.308, hydroxypropylmethylcellulose 1.018, Macrogol 0.644, talc 1.624, TiO2 0.950, indigo carmine color lacquer 0.170, polysorbate 80 0.034, and dimethicone 0.004 mg.

IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combination prepns. for treatment of cardiac and cardiovascular disorders)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L22 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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L23 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:312052 CAPLUS
DOCUMENT NUMBER: 135:127050
TITLE: Detection of low levels of the amorphous phase in crystalline pharmaceutical materials by thermally stimulated current spectrometry
AUTHOR(S): Venkatesh, Gopi M.; Barnett, Maria E.; Owusu-Fordjour, Charles; Galop, Marc
CORPORATE SOURCE: SB Pharmaceutical, Collegeville, PA, 19426, USA
SOURCE: Pharmaceutical Research (2001), 18(1), 98-103
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

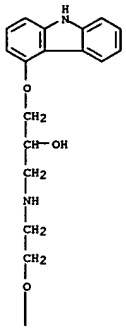
AB Purpose. To demonstrate the applicability of thermally stimulated current (TSC) spectrometry for the detection of low levels of the amorphous phase in crystalline pharmaceutical materials. Methods. A crystalline drug substance was melt quenched to produce an amorphous material. Blends of the crystalline and amorphous phases in different ratios (from 75:25 to 99:01) were prepared by serial dilution TSC studies were performed by applying an elec. field at a temperature above the glass transition temperature (Tg) to orient the dipoles, rapidly cooling to 0°, short circuiting for 1 min. and scanning at 7°/min to measure the depolarization current. The temperature of the peak in the spectrum corresponds to the Tg of the amorphous phase. Modulated DSC studies were performed by using 3 different test protocols (varying linear heating rate, modulation amplitude, and time period). Powder x-ray diffraction (XRD) studies were performed. Results. The ability to detect the amorphous phase by powder XRD is beset with problems due to indirect inference, orientation effects, and instrument-related intensity variations. Even using a consistent sampling procedure and an internal standard, the XRD could quantify the amorphous phase at a level of 5%. In the conventional or modulated DSC, the amorphous phase manifests itself as a shift in the baseline. Using modulated DSC it was possible to detect the amorphous phase at a level of 5% when tested at a heating rate of 2°/min and an amplitude of 1.0° with a period of 30 s. The moisture sorption method appears to have a similar detection capability. In TSC scans, the glass transition event due to mol./segmental mobility in the amorphous phase was manifested as a peak/shoulder on the low-temperature side of the depolarization peak of the crystalline phase. The amorphous phase was unambiguously detected at 2% with a lower detection limit of 1%. Conclusions. On the basis of the results of this preliminary investigation. TSC appears to be capable of detecting the amorphous phase at as low as 1% in crystalline pharmaceuticals, thus offering a much needed capability in discerning factors.

IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of low levels of amorphous phase in crystalline pharmaceuticals by thermally stimulated current spectrometry)

L23 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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L24 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1043923 CAPLUS
DOCUMENT NUMBER: 144:40569
TITLE: Development of novel interpenetrating network gellan gum-poly(vinyl alcohol) hydrogel microspheres for the controlled release of carvedilol
AUTHOR(S): Agnihotri, Sunil A.; Aminabhavi, Tejraj M.
CORPORATE SOURCE: Drug Delivery Division, Center of Excellence in Polymer Science, Karnatak University, Dharwad, India
SOURCE: Drug Development and Industrial Pharmacy (2005), 31(6), 491-503
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Taylor & Francis, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

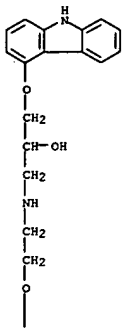
AB Novel interpenetrating polymeric network microspheres of gellan gum and poly(vinyl alc.) were prepared by the emulsion crosslinking method. Carvedilol, an antihypertensive drug, was successfully loaded into these microspheres prepared by changing the exptl. variables such as ratio of gellan gum:poly(vinyl alc.) and extent of crosslinking to optimize the process variables on drug encapsulation efficiency, release rates, size, and morphol. of the microspheres. Formation of interpenetrating network and the chemical stability of carvedilol after preparing the microspheres was confirmed by Fourier transform IR spectroscopy. Differential scanning calorimetry and x-ray diffraction studies were made on the drug-loaded microspheres to investigate the crystalline nature of the drug after encapsulation. Results indicated a crystalline dispersion of carvedilol in the polymer matrix. SEM confirmed the spherical nature and smooth surface morphol. of the microspheres produced. Mean particle size of the microspheres as measured by laser light scattering technique ranged between 230 and 346 μm. Carvedilol was successfully encapsulated up to 87% in the polymeric matrixes. In vitro release studies were performed in the simulated gastric fluid or simulated intestinal fluid. The release of carvedilol was continued up to 12 h. Dynamic swelling studies were performed in the simulated gastric fluid or simulated intestinal fluid, and diffusion coeffs. were calculated by considering the spherical geometry of the matrixes. The release data were fitted to an empirical relation to estimate the transport parameters. The mech. properties of interpenetrating polymeric networks prepared were investigated. Network parameters such as molar mass between cross-links and crosslinking d. for interpenetrating polymeric networks were calculated

IT 72956-09-3, Carvedilol
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(interpenetrating network gellan gum-poly(vinyl alc.) hydrogel microspheres for controlled release of carvedilol)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L24 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:20485 CAPLUS
DOCUMENT NUMBER: 140:82264
TITLE: Crystalline form of carvedilol hydrobromide for cardiovascular therapy
INVENTOR(S): Chen, Pingyun Y.; Dai, Qunying; Dell'orco, Phillip C.; Hisler, Claire; Igo, David H.; Katrincic, Lee M.; Labaw, Clifford S.; Ping, Li-jen
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004002472	A1	20040108	WO 2003-US20346	20030627
WO 2004002472	C1	20050224		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2492084	AA	20040108	CA 2003-2492084	20030627
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JP 2005533822	T2	20051110	JP 2004-517980	20030627
US 2005261355	A1	20051124	US 2004-518206	20041216
PRIORITY APPLN. INFO.:			US 2002-392374P P	20020627
			WO 2003-US20346 W	20030627

AB The present invention relates to a salt of carvedilol, corresponding compns. containing such a carvedilol salt or corresponding solvates thereof, and/or methods of using the aforementioned compound(s) in the treatment of certain disease states in mammals, in particular man. The present invention further relates to a novel crystalline form of carvedilol hydrobromide, which is the hydrobromide salt of 1-(carbazol-4-yloxy)-3-[[2-(methoxyphenoxy)ethyl]amino]-2-propanol, and/or other carvedilol solvates thereof, compns. containing salts or solvates of carvedilol hydrobromide, and methods of using the aforementioned compound(s) to treat hypertension, congestive heart failure, and angina, etc.

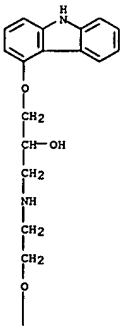
IT 374779-42-7DP, solvates 640724-11-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)

RN 374779-42-7 CAPLUS

L24 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



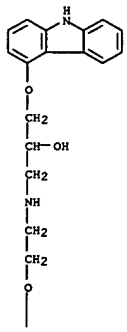
PAGE 2-A

● HBr

RN 640724-11-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

L24 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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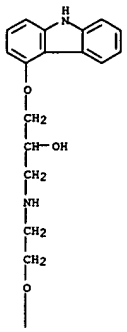
● HBr

● H_2O

IT 374779-42-7
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 374779-42-7 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide (9CI) (CA INDEX NAME)

L24 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



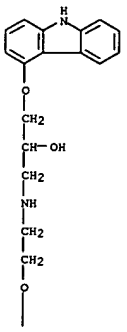
PAGE 2-A

● HBr

IT 72956-09-3, Carvedilol
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrobromination and hydration; crystalline form of carvedilol hydrobromide for cardiovascular therapy)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L24 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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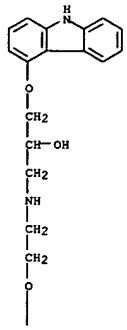
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:312052 CAPLUS
DOCUMENT NUMBER: 135:127050
TITLE: Detection of low levels of the amorphous phase in crystalline pharmaceutical materials by thermally stimulated current spectrometry
AUTHOR(S): Venkatesh, Gopi M.; Barnett, Maria E.; Owusu-Fordjour, Charles; Galop, Marc
CORPORATE SOURCE: SB Pharmaceutical, Collegeville, PA, 19426, USA
SOURCE: Pharmaceutical Research (2001), 18(1), 98-103
CODEN: PHREEB; ISSN: 0724-8741
PUBLISHER: Kluwer Academic/Plenum Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose. To demonstrate the applicability of thermally stimulated current (TSC) spectrometry for the detection of low levels of the amorphous phase in crystalline pharmaceutical materials. Methods. A crystalline drug substance was melt quenched to produce an amorphous material. Blends of the crystalline and amorphous phases in different ratios (from 75:25 to 99:01) were prepared by serial dilution TSC studies were performed by applying an elec. field at a temperature above the glass transition temperature (Tg) to orient the dipoles, rapidly cooling to 0°, short circuiting for 1 min. and scanning at 7°/min to measure the depolarization current. The temperature of the peak in the spectrum corresponds to the Tg of the amorphous phase. Modulated DSC studies were performed by using 3 different test protocols (varying linear heating rate, modulation amplitude, and time period). Powder x-ray diffraction (XRD) studies were performed. Results. The ability to detect the amorphous phase by powder XRD is beset with problems due to indirect inference, orientation effects, and instrument-related intensity variations. Even using a consistent sampling procedure and an internal standard, the XRD could quantify the amorphous phase at a level of 5%. In the conventional or modulated DSC, the amorphous phase manifests itself as a shift in the baseline. Using modulated DSC it was possible to detect the amorphous phase at a level of 5% when tested at a heating rate of 2°/min and an amplitude of 1.0° with a period of 30 s. The moisture sorption method appears to have a similar detection capability. In TSC scans, the glass transition event due to mol./segmental mobility in the amorphous phase was manifested as a peak/shoulder on the low-temperature side of the depolarization peak of the crystalline phase. The amorphous phase was unambiguously detected at 2% with a lower detection limit of 1%. Conclusions. On the basis of the results of this preliminary investigation. TSC appears to be capable of detecting the amorphous phase at as low as 1% in crystalline pharmaceuticals, thus offering a much needed capability in discerning factors.
IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(detection of low levels of amorphous phase in crystalline pharmaceuticals

L24 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
by thermally stimulated current spectrometry)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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L24 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:654214 CAPLUS
DOCUMENT NUMBER: 130:3743
TITLE: Synthesis and crystal structure of carvedilol
AUTHOR(S): Chen, Wei-Min; Zeng, Long-Mei; Yu, Kai-Bei; Xu, Ji-Hong
CORPORATE SOURCE: Inst. Pharmaceutical Sci., The First Military Med. Univ., Canton, 510515, Peop. Rep. China
SOURCE: Jiegou Huaxue (1998), 17(5), 325-328
CODEN: JHUADF; ISSN: 0254-5861
PUBLISHER: "Jiegou Huaxue" Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: English
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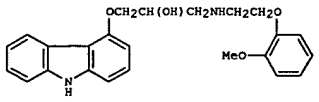

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AB The crystal structure of carvedilol (I), prepared from 4-(2,3-epoxypropoxy)carbazole and 2-MeOC6H4OCH2CH2NH2, was determined by single-crystal x-ray diffraction. The crystal is composed of a pair of enantiomers, and there are hydrogen bonds O-H-N between the two enantiomers. There are two planes in the mol.
IT 72956-09-3P, Carvedilol
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and crystal structure of)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L24 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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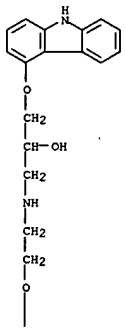

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FULL ESTIMATED COST	264.09	499.08

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-34.50	-34.50

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 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  FEB 27   New STN AnaVist pricing effective March 1, 2006
 NEWS  4  APR 04   STN AnaVist $500 visualization usage credit offered
 NEWS  5  MAY 10   CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS  6  MAY 11   KOREAPAT updates resume
 NEWS  7  MAY 19   Derwent World Patents Index to be reloaded and enhanced
 NEWS  8  MAY 30   IPC 8 Rolled-up Core codes added to CA/CAplus and
                   USPATFULL/USPAT2
 NEWS  9  MAY 30   The F-Term thesaurus is now available in CA/CAplus
 NEWS 10  JUN 02   The first reclassification of IPC codes now complete in
                   INPADOC
 NEWS 11  JUN 26   TULSA/TULSA2 reloaded and enhanced with new search and
                   and display fields
 NEWS 12  JUN 28   Price changes in full-text patent databases EPFULL and PCTFULL
 NEWS 13  JUl 11   CHEMSAFE reloaded and enhanced
 NEWS 14  JUl 14   FSTA enhanced with Japanese patents
 NEWS 15  JUl 19   Coverage of Research Disclosure reinstated in DWPI
 NEWS 16  AUG 09   INSPEC enhanced with 1898-1968 archive
 NEWS 17  AUG 28   ADISCTI Reloaded and Enhanced

 NEWS EXPRESS  JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
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 NEWS IPC8     For general information regarding STN implementation of IPC 8
 NEWS X25      X.25 communication option no longer available

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FILE 'HOME' ENTERED AT 08:57:57 ON 30 AUG 2006

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'REGISTRY' ENTERED AT 08:58:11 ON 30 AUG 2006
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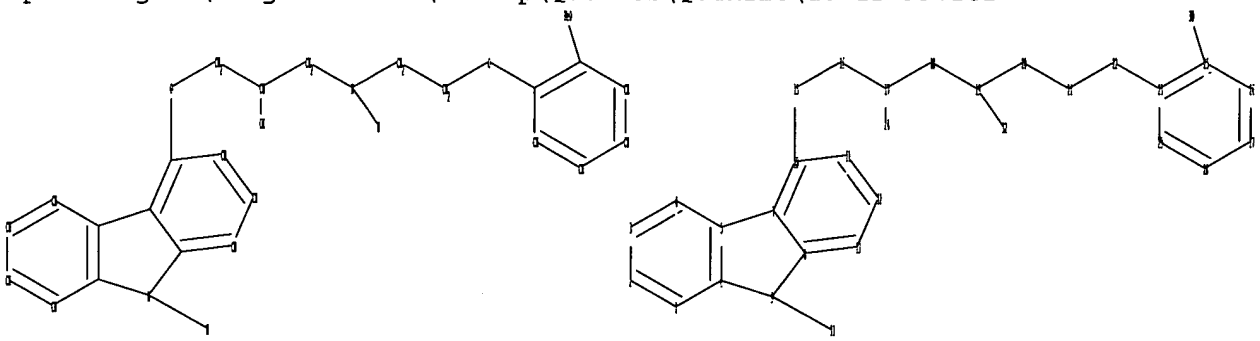

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ring nodes :
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25-30
ring bonds :
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23-25 23-29 25-26 26-27 27-28 28-29
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6-9 8-9 10-15 17-24 22-23
exact bonds :
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normalized bonds :
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isolated ring systems :
containing 1 : 23 :

Match level :
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11:Atom 12:Atom 13:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
20:CLASS 21:CLASS 22:CLASS 23:Atom 24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom
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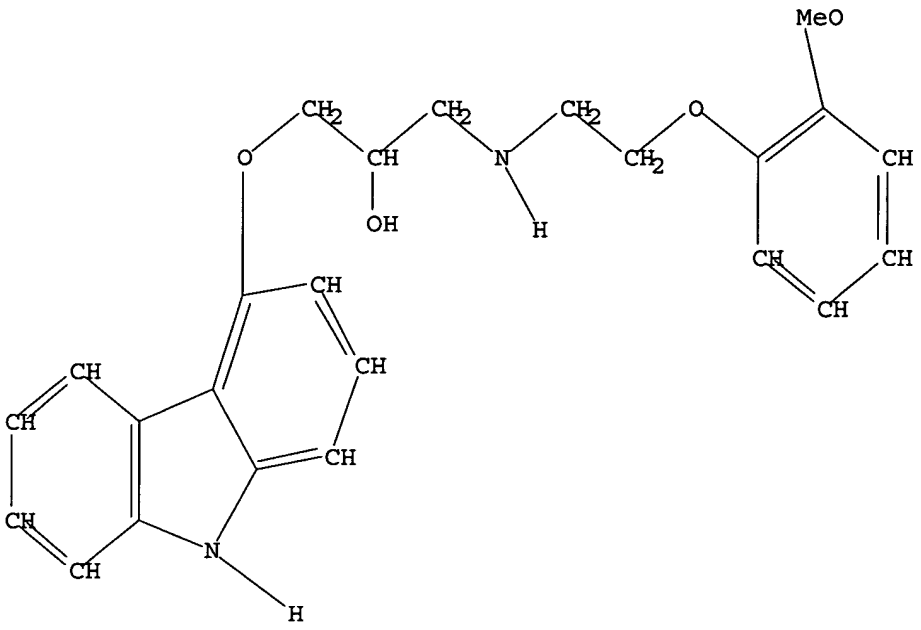


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SCREEN SEARCH COMPLETED -        7 TO ITERATE

100.0% PROCESSED         7 ITERATIONS                                 4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            7 TO      298
PROJECTED ANSWERS:               4 TO      200

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SEARCH TIME: 00.00.01

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=> fil caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
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FILE 'CAPLUS' ENTERED AT 08:58:34 ON 30 AUG 2006
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FILE COVERS 1907 - 30 Aug 2006 VOL 145 ISS 10
FILE LAST UPDATED: 29 Aug 2006 (20060829/ED)

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=> s l3
L4         1323 L3

=> s l4 and polymorph?
         192581 POLYMORPH?
L5           37 L4 AND POLYMORPH?

=> d ibib abs hitstr 1-37
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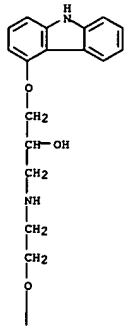
L5 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:782679 CAPLUS
TITLE: A polymorphism within a conserved β1-adrenergic receptor motif alters cardiac function and β-blocker response in human heart failure
AUTHOR(S): Liggett, Stephen B.; Mialet-Perez, Jeanne; Thaneemit-Chen, Surai; Weber, Stewart A.; Greene, Scott M.; Hodne, Danielle; Nelson, Bradley; Morrison, Jennifer; Domanski, Michael J.; Wagoner, Lynne E.; Abraham, William T.; Anderson, Jeffrey L.; Carlquist, John F.; Krause-Steinrauf, Heide J.; Lazzeroni, Laura C.; Port, J. David; Lavori, Philip W.; Bristow, Michael R.
CORPORATE SOURCE: Departments of Medicine and Physiology, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2006), 103(30), 11288-11293
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Heterogeneity of heart failure (HF) phenotypes indicates contributions from underlying common polymorphisms. We considered polymorphisms in the β1-adrenergic receptor (β1AR), a β-blocker target, as candidate pharmacogenomic loci. Transfected cells, genotyped human nonfailing and failing ventricles, and a clin. trial were used to ascertain phenotype and mechanism. In non-failing and failing isolated ventricles, β1-Arg-389 had resp. 2.8±0.3- and 4.3±2.1-fold greater agonist-promoted contractility vs. β1-Gly-389, defining enhanced physiol. coupling under relevant conditions of endogenous expression and HF. The β-blocker bucindolol was an inverse agonist in failing Arg, but not Gly, ventricles, without partial agonist activity at either receptor; carvedilol was a genotype-independent neutral antagonist. In transfected cells, bucindolol antagonized agonist-stimulated cAMP, with a greater absolute decrease observed for Arg-389 (435±80 vs. 115±23 fmol per well). Potential pathophysiol. correlates were assessed in a placebo-controlled trial of bucindolol in 1040 HF patients. No outcome was associated with genotype in the placebo group, indicating little impact on the natural course of HF. However, the Arg-389 homozygotes treated with bucindolol had an age-, sex-, and race-adjusted 38% reduction in mortality (P = 0.03) and 34% reduction in mortality or hospitalization (P = 0.004) vs. placebo. In contrast, Gly-389 carriers had no clin. response to bucindolol compared with placebo. Those with Arg-389 and high baseline norepinephrine levels trended toward improved survival, but no advantage with this allele and exaggerated sympatholysis was identified. We conclude that β1AR-389 variation alters signaling in multiple models and affects the β-blocker therapeutic response in HF and, thus, might be used to individualize treatment of the syndrome.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphism within a conserved β1-adrenergic receptor motif alters cardiac function and β-blocker response in human heart failure)

L5 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:558278 CAPLUS
DOCUMENT NUMBER: 145:62782
TITLE: Process for the preparation of carvedilol or its enantiomers from the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole or its enantiomers with an excess of 2-(2-methoxyphenoxy)ethylamine in ethyl acetate as the reaction solvent
INVENTOR(S): Trepat Guixer, Elisenda; Munoz Alvarez, Anna; Pomares Marco, Marta; Marquillas Olondriz, Francisco
PATENT ASSIGNEE(S): Zambon Group S.p.A., Italy
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006061364	A1	20060615	WO 2005-EP56469	20051205

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: EP 2004-106438 A 20041209

OTHER SOURCE(S): CASREACT 145:62782

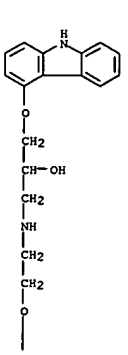
AB A process for the preparation of carvedilol, as well as its optically active R and S enantiomers, comprises the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole, or its enantiomers, with an excess of 2-(2-methoxyphenoxy)ethylamine using Et acetate as the reaction solvent.

IT 72956-09-3P, Carvedilol 95093-99-5P, (R)-Carvedilol 95094-00-1P, (S)-Carvedilol
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation of carvedilol or its enantiomers from the ring-opening reaction of 4-(2,3-epoxypropoxy)carbazole or its enantiomers with an excess of 2-(2-methoxyphenoxy)ethylamine in Et acetate as the reaction solvent)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

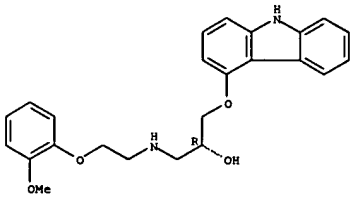


PAGE 2-A

RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

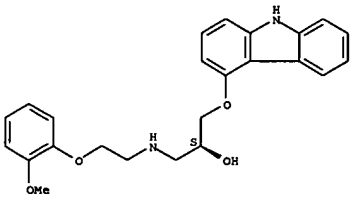
Absolute stereochemistry.

L5 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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L5 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:477158 CAPLUS
DOCUMENT NUMBER: 145:180148
TITLE: Multiple regression analysis of pharmacogenetic variability of carvedilol disposition in 54 healthy Japanese volunteers
AUTHOR(S): Honda, Mutsuko; Ogura, Yumi; Toyoda, Wakako; Taguchi, Masato; Nozawa, Takashi; Inoue, Hiroshi; Hashimoto, Yukiya
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, University of Toyama, 2630 Sugitani, Toyama, 930-0194, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2006), 29(4), 772-778
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

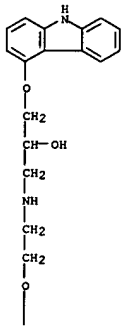
AB The aim of this study was to evaluate the pharmacogenetic variability in the disposition of carvedilol in the Japanese population. Five or 10 mg of carvedilol was orally administered to 54 healthy Japanese subjects (22-44 years old), and blood samples were taken at 2 and 6 h after dosing.
The authors determined the polymorphic alleles of CYP2D6, CYP2C9, CYP2C19, CYP3A5, UGT2B7, and MDR1 in each subject. The whole blood concentration
of R- and S-carvedilol was measured by an HPLC method. The pharmacokinetic parameters in individual subjects were estimated by the Bayesian method using the nonlinear mixed effects model (NONMEM) program. The authors then examined the effect of the genetic polymorphisms on the variability in the pharmacokinetics of carvedilol using a multiple regression anal. The oral clearance (CL/F) and also apparent volume of distribution (V/F) of both enantiomers were significantly lower in the subjects with the CYP2D6*10 allele than those with the CYP2D6*1/*1, *1/*2,
or *2/*2 genotype, confirming our previous finding that the bioavailability (F) and systemic clearance (CL) of R- and S-carvedilol in the liver is significantly altered in Japanese with the CYP2D6*10 allele. On the other hand, CYP2C9*3, CYP2C19*2, CYP2C19*3, CYP3A5*3, UGT2B7*2, and
MDR1 C3435T did not significantly affect the pharmacokinetics of carvedilol in Japanese subjects.

IT 72956-09-3, Carvedilol 95093-99-5, R-Carvedilol
95094-00-1, S-Carvedilol
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(multiple regression anal. of pharmacogenetic variability of carvedilol
disposition in 54 healthy Japanese volunteers)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-
(9CI) (CA INDEX NAME)

L5 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A

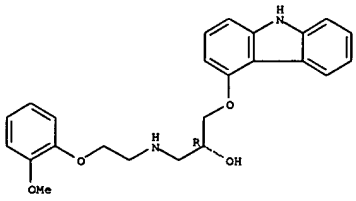


PAGE 2-A

RN 95093-99-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2R)- (9CI) (CA INDEX NAME)

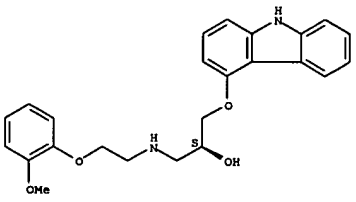
Absolute stereochemistry.

L5 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS
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L5 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:384143 CAPLUS
DOCUMENT NUMBER: 145:75973
TITLE: Contribution of polymorphisms in UDP-glucuronosyltransferase and CYP2D6 to the individual variation in disposition of carvedilol
AUTHOR(S): Takekuma, Yoh; Takenaka, Toru; Kiyokawa, Masami; Yamazaki, Koujiro; Okamoto, Hiroshi; Kitabatake, Akira; Tsutsui, Hiroyuki; Sugawara, Mitsuru
CORPORATE SOURCE: Department of Clinical Pharmaceutics and Therapeutics, Graduate School of Pharmaceutical Science, Hokkaido University, Sapporo, Japan
SOURCE: Journal of Pharmacy & Pharmaceutical Sciences (2006), 9(1), 101-112
CODEN: JPPSFY; ISSN: 1482-1826
URL: http://www.ualberta.ca/~csps/JPPS9(1)/Karimi.G/LP S.pdf
PUBLISHER: Canadian Society for Pharmaceutical Sciences
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English

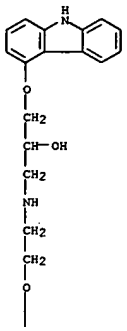
AB Purpose: It has been reported that carvedilol, which has beta-adrenergic blocking and vasodilating activities, is mainly metabolized by UDP-glucuronosyltransferase (UGT) 1A1, UGT2B4, UGT2B7 and CYP2D6. The aim of this study was to determine whether the activity of glucuronidation has an influence on the area under the curve (AUC) of carvedilol and whether polymorphisms in UGTs and CYP2D6 contribute to individual variation in disposition of carvedilol in Japanese. Methods: Plasma concns. of carvedilol and its glucuronide were determined by reversed-phase high-performance liquid chromatog. (HPLC). Genotyping of UGT1A1, UGT2B4 and UGT2B7 genes was carried out by the direct sequence method. CYP2D6 genotyping was carried out using an amplification refractory mutation system (ARMS) assay and PCR-restriction fragment length polymorphism (RFLP). Results: The level of carvedilol glucuronidation ability in the high-level AUC group was significantly lower than that in the low-level group. The frequencies of UGT1A1*6, UGT2B7*3 and CYP2D6*10 in the low level ability of glucuronidation group were significantly higher than those in the high level group, and the same tendency was found in the frequency of CYP2D6*5, though there was no significant difference. Conclusion: Polymorphisms of UGT1A1, UGT2B7 and CYP2D6 strongly affect the pharmacokinetics and disposition of carvedilol in Japanese.

IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glucuronidation ability of carvedilol was lower in patient with high-compared to low-level of carvedilol AUC, whereas frequency of UGTA1*6, UGT2B7*3 and CYP2D6*10 was higher in patient with low compared to high ability of glucuronidation)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1154373 CAPLUS
DOCUMENT NUMBER: 143:416239
TITLE: Combination of (S)-amlodipine and a beta-blocker, and methods for reducing hypertension
INVENTOR(S): Bush, Larry; Grogan, Donna Roy
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005099699	A1	20051027	WO 2005-US10485	20050329

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-560069P P 20040407

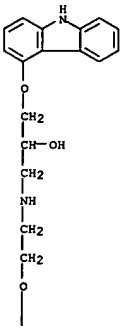
AB One aspect of the present invention relates to pharmaceutical compns. comprising optically pure (S)-amlodipine and a beta-blocker. In a preferred embodiment, the beta-blocker is atenolol or bisoprolol. Another aspect of the present invention relates to pharmaceutical compns. consisting essentially of at least one pharmaceutically acceptable carrier, optically pure (S)-amlodipine and a beta-blocker. In a preferred embodiment, the beta-blocker is atenolol or bisoprolol. The pharmaceutical compns. of the invention are useful, e.g., in the treatment of hypertension. In addition, the present invention also relates to a method of treating a patient suffering from hypertension or a related cardiac disorder, comprising co-administering to a patient in need thereof a therapeutically effective amount of optically pure (S)-amlodipine and a beta-blocker. In certain embodiments of the compns. and methods, said optically pure (S)-amlodipine is optically pure (S)-amlodipine malate, or a polymorph, pseudopolymorph or solvate thereof.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of amlodipine and beta-blocker for reducing hypertension)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1018044 CAPLUS
DOCUMENT NUMBER: 143:278382
TITLE: Effect of CYP2D6*10 on the pharmacokinetics of R- and S-carvedilol in healthy Japanese volunteers
AUTHOR(S): Honda, Mutsuko; Nozawa, Takashi; Igarashi, Norio; Inoue, Hiroshi; Arakawa, Rie; Ogura, Yumi; Okabe, Hiromi; Taguchi, Masato; Hashimoto, Yukiya
CORPORATE SOURCE: Graduate School of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama, 930-0194, Japan
SOURCE: Biological & Pharmaceutical Bulletin (2005), 28(8), 1476-1479
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

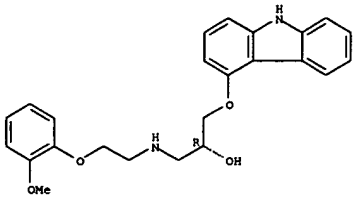
AB This study was performed to investigate the effect of CYP2D6*10 on the pharmacokinetics of R- and S-carvedilol in healthy Japanese volunteers. Five or 10 mg of carvedilol was orally administered to 23 subjects (22-44 years old), and blood samples were taken at 2 and 6 h after dosing. We determined the polymorphic alleles of CYP2D6 in each subject. The whole blood concentration of R- and S-carvedilol was measured by an HPLC method. The pharmacokinetic parameters in individual subjects were estimated by the Bayesian method using the nonlinear mixed effects model (NONMEM) program. The mean values of oral clearance for R- and S-carvedilol were estimated to be 1.01 and 2.15 l/h/kg, resp. The oral clearance was highly correlated with the apparent volume of distribution among the subjects, suggesting that the interindividual difference in bioavailability was largely responsible for the pharmacokinetic variability of carvedilol. The oral clearance and also volume of distribution of both enantiomers were significantly lower in the subjects with the CYP2D6*10 allele than with the CYP2D6*1/*1 or *1/*2 genotype. These results suggested that the systemic and/or pre-systemic metabolism of R- and S-carvedilol in the liver is significantly decreased in Japanese with the CYP2D6*10 allele.

IT 95093-99-5, R-Carvedilol 95094-00-1, S-Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of CYP2D6*10 on pharmacokinetics of R- and S-carvedilol in healthy volunteers)

RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

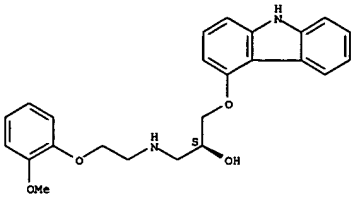
Absolute stereochemistry.

L5 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:645868 CAPLUS
DOCUMENT NUMBER: 143:205611
TITLE: Oxidative-nitrosative stress in hypertension
AUTHOR(S): Escobales, Nelson; Crespo, Maria J.
CORPORATE SOURCE: Department of Physiology, School of Medicine, University of Puerto Rico, San Juan, P. R.
SOURCE: Current Vascular Pharmacology (2005), 3(3), 231-246
CODEN: CVPUAY; ISSN: 1570-1611
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Reactive oxygen species (ROS) are important signaling mols. in the vasculature. However, when there is imbalance between their occurrence and antioxidant defense mechanisms, ROS can contribute to the vascular abnormalities that lead to hypertension. Evidence accumulated in the last decade strongly supports the notion that ROS are generated in the vasculature mainly by NAD(P)H oxidase in a mechanism that is angiotensin II-dependent. Activation of this enzyme leads to superoxide production and uncouples endothedial NO synthase (eNOS), which sustains oxidative stress while increasing the levels of tissue-damaging peroxynitrite. The latter can result in vascular dysfunction. NAD(P)H-dependent ROS formation, in particular H2O2, could also contribute to vascular injury by sustaining NAD(P)H oxidase activation, promoting inflammatory gene expression, extracellular matrix reorganization, and growth (hypertrophy/hyperplasia) of vascular smooth muscle cells. The effect of ROS appears to be mediated by redox-sensitive targets such as tyrosine kinases and phosphatases, mitogen-activated protein kinases, transcription factors, matrix metalloproteinases, peroxisome proliferator activated receptor-α, poly(ADP-ribose)polymerase-1, Ca2+ signaling mechanisms and secreted factors such as cyclophilin A and heat shock protein 90-α. Redox-sensitive targets appear to play a central role in normal vascular function, but can also lead to remodeling of the vascular wall, increasing vascular reactivity and hypertension. Polymorphisms in the p22phox gene promoter could determine susceptibility to NAD(P)H-mediated oxidative stress in humans and animals with hypertension. Although ROS are strongly implicated in the etiol. of hypertension, clin. trials with antioxidants are inconclusive regarding their effectiveness in treating the disease. New drugs with both antihypertensive action and antioxidant properties (Celiprolol, Carvedilol) offer promising results in the management of hypertension.

IT 72956-09-3, Carvedilol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oxidative-nitrosative stress and pharmacol. of hypertension)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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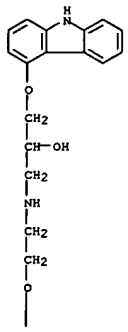

PAGE 2-A

REFERENCE COUNT: 232 THERE ARE 232 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:638703 CAPLUS
DOCUMENT NUMBER: 143:139194
TITLE: Buccal dosage forms for extended drug release
INVENTOR(S): Jain, Rajesh; Jindal, Kour Chand; Singh, Sukhjeet
PATENT ASSIGNEE(S): Panacea Biotec Ltd., India
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005065640	A1	20050721	WO 2005-IN3	20050105
WO 2005065640	C1	20051208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: IN 2004-DE24 A 20040106
IN 2004-DE26 A 20040106

AB Buccal dosage form compns., preferably of poorly bioavailable drug(s), or drug(s) which undergo extensive presystematic metabolism, are provided. The compns. provide extended release of the drug in the oral cavity, and are preferably in the taste masked form. A process of preparing of such compns. is also provided. Thus, a tablet contained sumatriptan succinate 25.0, Indion-204 75.0, maltodextrin 48.0, sucrose 30.0, CM-cellulose 18.0, HPMC 8.0, HPC 8.0, citric acid 15.0, NaCl 5.0, and Povidone 3.0 25 mg/tablet.

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(buccal dosage forms for extended drug release)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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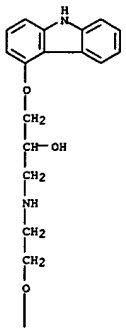


PAGE 2-A

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:493479 CAPLUS
DOCUMENT NUMBER: 143:32328
TITLE: Carvedilol free base, salts and solvates for controlled release formulations for treatment of cardiovascular diseases
INVENTOR(S): Burke, Matthew D.; Lamey, Kimberly A.; Martini, Luigi G.; Oh, Choon; Peterson, Heather; Staton, Jeffrey Scott; Zhang, Lihua; Coffin, Mark Davis
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.
SOURCE: PCT Int. Appl., 248 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051325	A2	20050609	WO 2004-US39677	20041124
WO 2005051325	A3	20050811		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1686967	A2	20060809	EP 2004-812238	20041124

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS

PRIORITY APPLN. INFO.: US 2003-524991P P 20031125
WO 2004-US39677 W 20041124

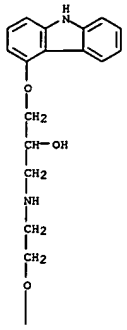
AB The present invention relates to carvedilol free base, salts, anhydrous forms, or solvates thereof, corresponding pharmaceutical compns. or controlled release formulations, and methods for delivery of carvedilol forms to the lower gastrointestinal tract or methods to treat cardiovascular diseases, which may include, but are not limited to hypertension, congestive heart failure, and angina. Thus, carvedilol monocitrate monohydrate was prepared by reaction of 100 g 20% citric acid solution and 2.2 g carvedilol and overnight evaporation giving large single crystals. Also, controlled-release carvedilol tablets were prepared by spray coating a core. The core comprised carvedilol phosphate hemihydrate 41.4, mannitol 261.6,, Hypromellose 120.4, microcryst. cellulose 120.6, Povidone 47, colloidal silica 6.0, and Mg stearate 6.0 mg. The cores were spray coated by an aqueous suspension containing (per tablet) Opadry II Color 12.1, Eudragit L30 D-55 39.2, tri-Et citrate 4.0, glyceryl stearate 1.3, and Polysorbate 80 4.0 mg.

IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(oral controlled-release carvedilol free base and salts and solvates for in treatment of cardiovascular diseases)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

IT 340269-63-8P 374779-41-6P 374779-42-7P
374779-43-8P 374779-45-0P 374779-53-0P
374779-87-0P 610309-89-2P 623113-70-2P
640724-11-4P 641571-35-9P 787598-89-4P,
Carvedilol oxalate 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P
852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P 852995-90-5P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(oral controlled-release carvedilol free base and salts and solvates for in treatment of cardiovascular diseases)

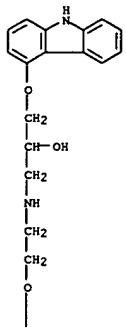
RN 340269-63-8 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

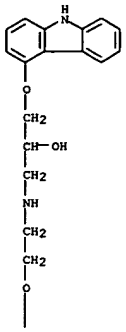
CM 2

CRN 75-75-2
CMF C H4 O3 S

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

PAGE 1-A



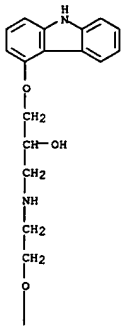
PAGE 2-A

● HCl

RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

● HBr

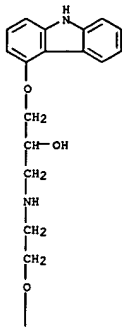
RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

CM 2

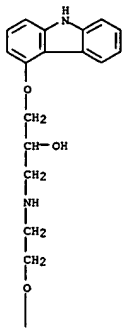
CRN 7664-93-9
CMF H2 O4 S

RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

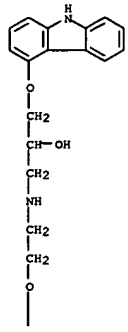
RN 374779-53-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

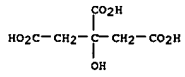
PAGE 1-A



PAGE 2-A

CM 2

CRN 77-92-9
CMF C6 H8 O7



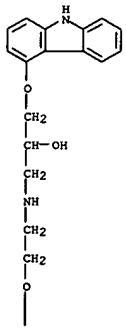
RN 374779-87-0 CAPLUS

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



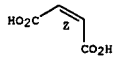
PAGE 2-A

CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

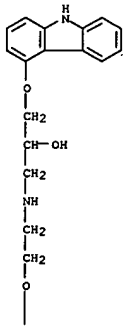


RN 610309-89-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CMF H3 O4 P

RN 623113-70-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI)
(CA
INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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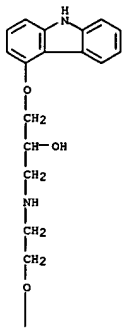


PAGE 2-A

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

● HBr

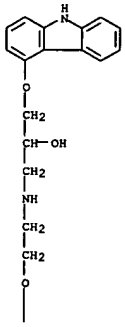
● H_2O

RN 641571-35-9 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

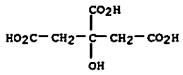
PAGE 1-A



L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

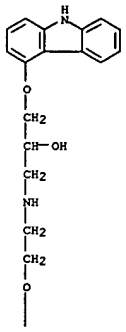
CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 2-A

CM 2

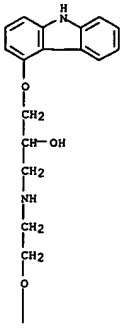
CRN 7664-38-2
CMF H3 O4 P

RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

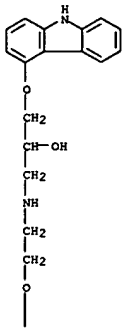
CRN 144-62-7
CMF C2 H2 O4

RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

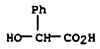
PAGE 1-A



PAGE 2-A

CM 2

CRN 90-64-2
CMF C8 H8 O3

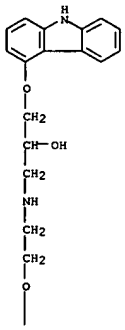


RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

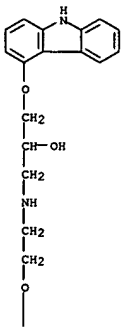
CRN 50-21-5
CMF C3 H6 O3

RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

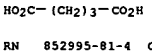
PAGE 1-A



PAGE 2-A

CM 2

CRN 110-94-1
CMF C5 H8 O4



RN 852995-81-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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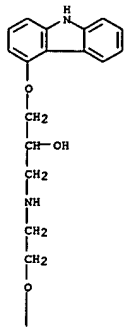

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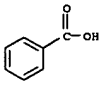
CM 2

CRN 65-85-0
CMF C7 H6 O2



RN 852995-82-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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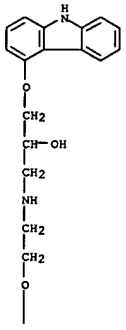

PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

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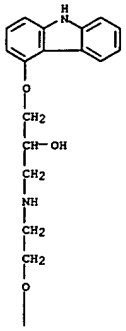

PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 3

CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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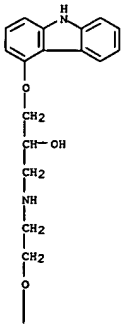

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CM 2

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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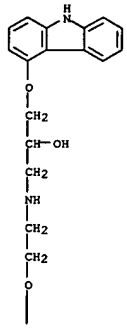


PAGE 2-A

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 71-41-0
CMF C5 H12 O

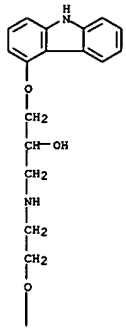
Me—(CH2)4—OH

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

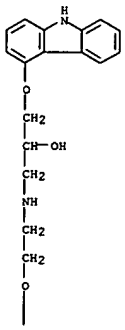
CRN 78-83-1
CMF C4 H10 O

RN 852995-87-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

L5 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 75-89-8
CMF C2 H3 F3 O

F3C—CH2—OH

RN 852995-88-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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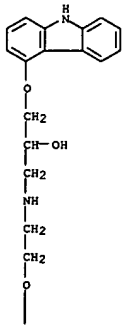

PAGE 2-A

CM 2

CRN 67-63-0
CMF C3 H8 O

RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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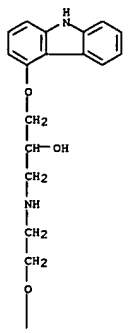

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CM 2

CRN 71-23-8
CMF C3 H8 O

RN 852995-90-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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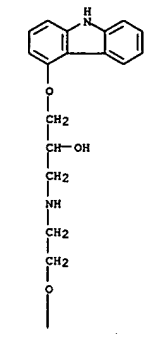
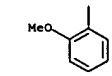


PAGE 2-A



CM 2

CRN 64-17-5
CMF C2 H6 O

ACCESSION NUMBER: 2005:490290 CAPLUS
DOCUMENT NUMBER: 143:32320
TITLE: Carvedilol salts and solvates and corresponding compositions for treatment of cardiovascular diseases
INVENTOR(S): Brook, Christopher S.; Chen, Pingyun Y.; Chen, Wei; Dai, Qunying; Dell'Orco, Philip C.; Hisler, Claire; Igo, David H.; Katrincic, Lee M.; Labaw, Clifford S.; Louvet, Ann Marie; Oh, Choon K.; Ping, Li-Jen; Spoors, Paul G.; Wang, Jun; Werner, Christopher
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., USA
SOURCE: PCT Int. Appl., 196 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051383	A1	20050609	WO 2004-US39528	20041124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005277689	A1	20051215	US 2004-997230	20041124
EP 1686986	A1	20060809	EP 2004-812113	20041124
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PRIORITY APPLN. INFO.: US 2003-524921P P 20031125
WO 2004-US39528 W 20041124

AB The present invention relates to a salt of carvedilol and/or corresponding solvates thereof, compns. containing such carvedilol and/or corresponding solvates thereof, and/or methods of using the aforementioned compound(s) in the treatment of certain disease states in mammals, in particular man. The present invention further relates to carvedilol phosphate salts, and/or solvates thereof, which include a novel crystalline form of carvedilol dihydrogen phosphate, and/or carvedilol hydrogen phosphate, and/or other corresponding solvates thereof, compns. containing these carvedilol salts and/or solvates, and methods of using these compds. to treat hypertension, congestive heart failure, angina, etc. Thus, carvedilol dihydrogen phosphate hemihydrate Form I was prepared from a reaction mixture of carvedilol and H3PO4 in acetone by adding seeds of carvedilol dihydrogen phosphate. Also, the pharmacokinetic study in dogs showed that oral bioavailability from carvedilol base in the small intestine is constrained by its low solubility at neutral pH. When oral units were introduced to the

stomach, the low gastric pH can be expected to facilitate dissoln. and absorption but this will not be the case in the more neutral small intestine or beyond. Thus, salts of carvedilol (carvedilol hydrobromide, phosphate and citrate) were formulated by using conventional (non-solubilizing) excipients such that drug did not become available until units were beyond the gastric milieu. Drug administered in salt form was rapidly and more completely absorbed than the free base form.

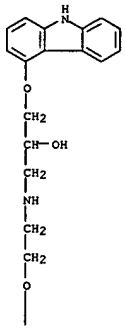
IT 340269-63-8P 374779-41-6P 374779-42-7P
374779-43-8P 374779-45-0P 374779-53-0P
374779-87-0P 610309-89-2P 623113-70-2P
640724-11-4P 641571-35-9P 787598-89-4P,
Carvedilol oxalate 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P
852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P 852995-90-5P
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(carvedilol salts and solvates for oral compns. with improved bioavailability for treatment of cardiovascular diseases)

RN 340269-63-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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● HCl

RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

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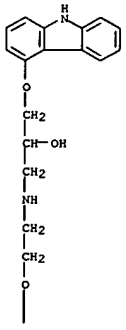

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● HBr

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CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

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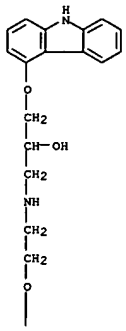

RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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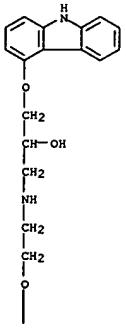

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CM 2

CRN 7664-93-9
CMF H2 O4 S

RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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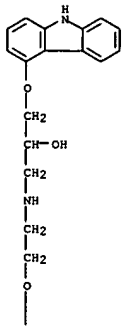

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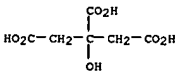
CM 2

CM 2

CRN 77-92-9
CMF C6 H8 O7

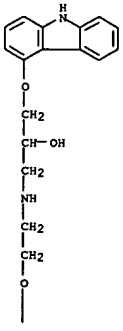


RN 374779-87-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



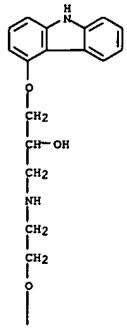
CRN 7664-38-2
CMF H3 O4 P

RN 374779-53-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



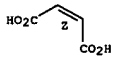
PAGE 2-A

PAGE 2-A

CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

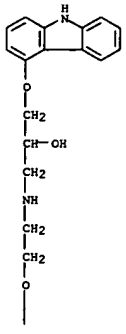


RN 610309-89-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

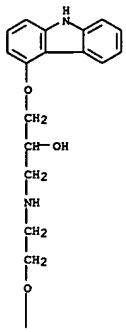
CRN 7664-38-2
CMF H3 O4 P

RN 623113-70-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI)
(CA
INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

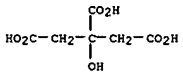
PAGE 1-A



PAGE 2-A

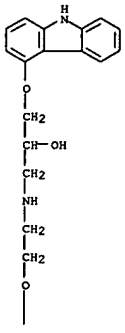
CM 2

CRN 77-92-9
CMF C6 H8 O7



RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

● HBr

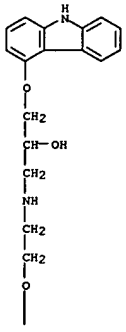
● H_2O

RN 641571-35-9 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

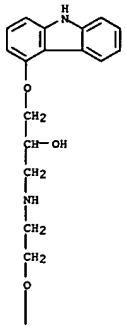
RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 144-62-7
CMF C2 H2 O4

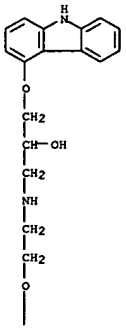
RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

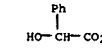
PAGE 1-A



PAGE 2-A

CM 2

CRN 90-64-2
CMF C8 H8 O3



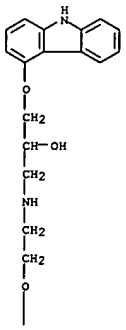
RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 50-21-5
CMF C3 H6 O3

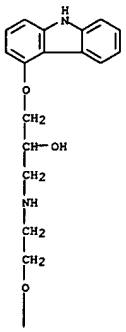
RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

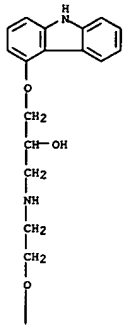
CRN 110-94-1
CMF C5 H8 O4

RN 852995-81-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

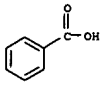
PAGE 1-A



PAGE 2-A

CM 2

CRN 65-85-0
CMF C7 H6 O2



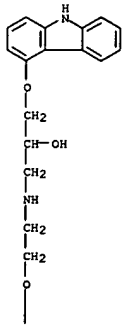
RN 852995-82-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

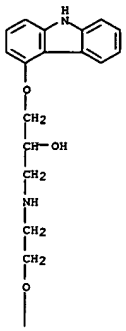
CRN 7664-38-2
CMF H3 O4 P

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

L5 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 3

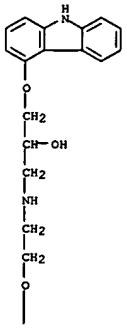
CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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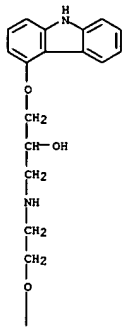

PAGE 2-A

CM 2

CRN 71-41-0
CMF C5 H12 O

$Me-(CH_2)_4-OH$

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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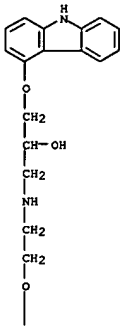


PAGE 2-A

CM 2

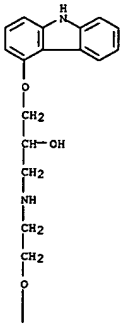
CRN 78-83-1
CMF C4 H10 O

RN 852995-87-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 75-89-8
CMF C2 H3 F3 O

F_3C-CH_2-OH

RN 852995-88-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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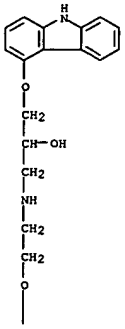


PAGE 2-A

CM 2

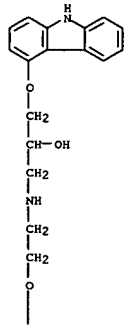
CRN 67-63-0
CMF C3 H8 O

RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



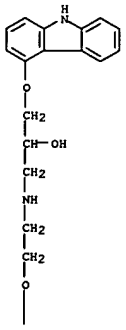
PAGE 2-A

CM 2

CRN 64-17-5
CMF C2 H6 O

IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(carvedilol salts and solvates for oral compns. with improved bioavailability for treatment of cardiovascular diseases)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

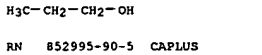
PAGE 1-A



PAGE 2-A

CM 2

CRN 71-23-8
CMF C3 H8 O

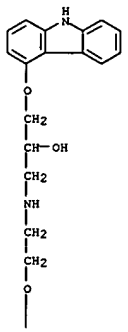


RN 852995-90-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:490272 CAPLUS
DOCUMENT NUMBER: 143:48055
TITLE: Controlled release pharmaceuticals containing carvedilol, its salts, or solvates
INVENTOR(S): Castan, Catherine; Crowley, Patrick J.; Guimberteau, Florence; Meyrueix, Remi; Oh, Choon; Soula, Gerard
PATENT ASSIGNEE(S): SB Pharmco Puerto Rico Inc., P. R.; Flamel Technologies
SOURCE: PCT Int. Appl., 287 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005051322	A2	20050609	WO 2004-US39614	20041124
WO 2005051322	A3	20060420		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2547137	AA	20050609	CA 2004-2547137	20041124
US 2005175695	A1	20050811	US 2004-997836	20041124
US 2005196459	A1	20050908	US 2004-996780	20041124
EP 1691789	A2	20060823	EP 2004-812185	20041124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU				

PRIORITY APPLN. INFO.: US 2003-524991P P 20031125
US 2004-605680P P 20040830
WO 2004-US39614 W 20041124

AB The present invention also relates to carvedilol free base, its salts, anhydrous forms, or solvates, corresponding controlled release formulations, and delivery or dosing methods of carvedilol forms to the lower gastrointestinal tract or methods to treat cardiovascular diseases, which may include, but are not limited to hypertension, congestive heart failure, atherosclerosis, and angina. The present invention relates to controlled release formulations, which comprise various carvedilol forms, which may include, but are not limited to a carvedilol free base or corresponding carvedilol salts, anhydrous forms or solvates thereof. Thus, carvedilol dihydrogen phosphate dihydrate was prepared by dissolving carvedilol dihydrogen phosphate in acetone/water mixture and removing acetone.

IT 374779-53-0P 623113-70-2P
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation);

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals contg. carvedilol or its salts or solvates)

RN 374779-53-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-{[2-(2-methoxyphenoxy)ethyl]amino}-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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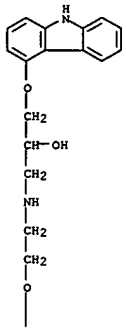

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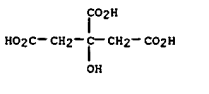
CM 2

CRN 77-92-9
CMF C6 H8 O7

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

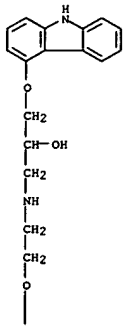


RN 623113-70-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, 2-hydroxy-1,2,3-propanetricarboxylate (1:1) (salt), monohydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A

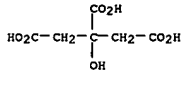


PAGE 2-A

CM 2

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

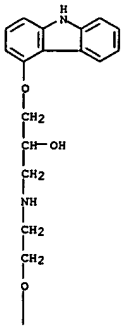
CRN 77-92-9
CMF C6 H8 O7



IT 72956-09-3
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or solvates)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino)-(9CI) (CA INDEX NAME)

PAGE 1-A



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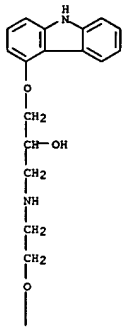
L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT 374779-42-7P 640724-11-4P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or solvates)
RN 374779-42-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide (9CI) (CA INDEX NAME)

PAGE 1-A



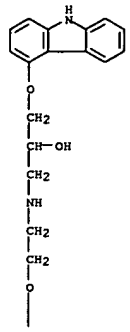
PAGE 2-A

● HBr

RN 640724-11-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, monohydrate (9CI) (CA INDEX NAME)

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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● HBr

● H_2O

IT 374779-45-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(controlled release pharmaceuticals containing carvedilol or its salts or solvates)
RN 374779-45-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 72956-09-3
CMF C24 H26 N2 O4

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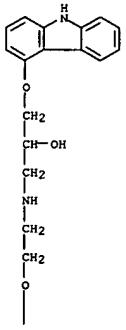


PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

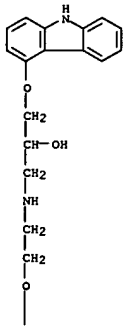
L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT 374779-43-8P 374779-87-0P 610309-89-2P
641571-35-9P 852995-78-9P 852995-79-0P
852995-80-3P 852995-81-4P 852995-82-5P
852995-83-6P 852995-84-7P 852995-85-8P,
biological studies 852995-86-9P 852995-87-0P
852995-88-1P 852995-89-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(controlled release pharmaceuticals contg. carvedilol or its salts or solvates)
RN 374779-43-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
sulfate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



PAGE 2-A

CM 2

CRN 7664-93-9

CMF H2 O4 S

RN 374779-87-0 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
(2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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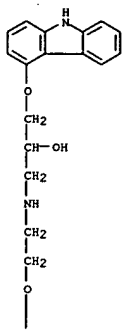

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CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 641571-35-9 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (1:1) (salt), dihydrate (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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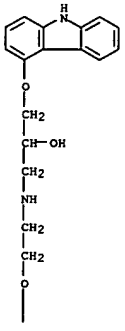
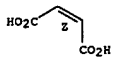


CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



RN 610309-89-2 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), hydrate (2:2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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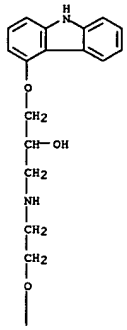

PAGE 2-A

CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 852995-78-9 CAPLUS
CN Benzeneacetic acid, α-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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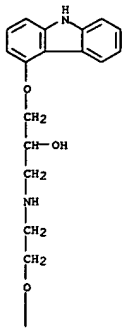

PAGE 2-A

CM 2

CRN 90-64-2
CMF C8 H8 O3

RN 852995-79-0 CAPLUS
CN Propanoic acid, 2-hydroxy-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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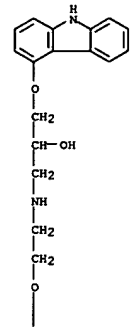

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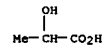
CM 2

CRN 50-21-5
CMF C3 H6 O3



RN 852995-80-3 CAPLUS
CN Pentanedioic acid, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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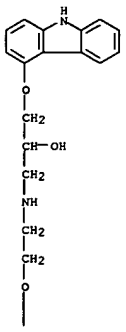

PAGE 2-A

CM 2

CRN 110-94-1
CMF C5 H8 O4

RN 852995-81-4 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monobenzoate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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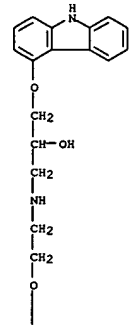

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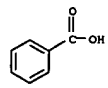
CM 2

CRN 65-85-0
CMF C7 H6 O2



RN 852995-82-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, phosphate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CRN 72956-09-3
CMF C24 H26 N2 O4

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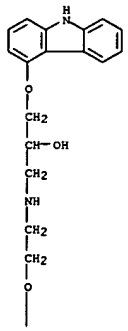

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CM 2

CRN 7664-38-2
CMF H3 O4 P

RN 852995-83-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
phosphate (salt), compd. with methanol (1:1:?) (9CI) (CA INDEX NAME)

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CM 3

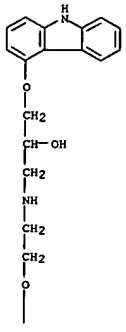
CRN 67-56-1
CMF C H4 O

RN 852995-84-7 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with 1,4-dioxane (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

PAGE 1-A



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CM 2

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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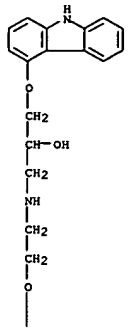

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CM 2

CRN 7664-38-2
CMF H3 O4 P

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CRN 123-91-1
CMF C4 H8 O2

RN 852995-85-8 CAPLUS
CN 1-Pentanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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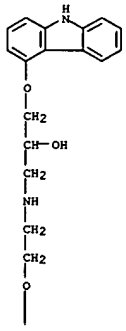

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L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 71-41-0
CMF C5 H12 O

RN 852995-86-9 CAPLUS
CN 1-Propanol, 2-methyl-, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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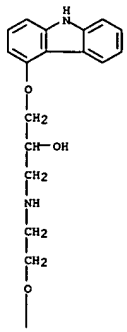

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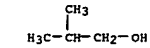
L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 78-83-1
CMF C4 H10 O



RN 852995-87-0 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2,2,2-trifluoroethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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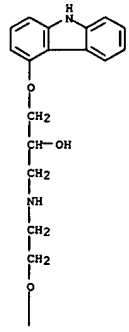

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L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 75-89-8
CMF C2 H3 F3 O

RN 852995-88-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, monohydrobromide, compd. with 2-propanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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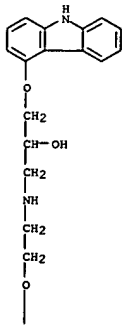

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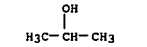
L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CM 2

CRN 67-63-0
CMF C3 H8 O



RN 852995-89-2 CAPLUS
CN 1-Propanol, compd. with 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-2-propanol monohydrobromide (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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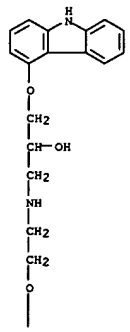

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CM 2

CRN 71-23-8
CMF C3 H8 O

IT 340269-63-8 374779-41-6 787598-89-4,
Carvedilol oxalate 852995-90-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceuticals containing carvedilol or its salts or
solvates)
RN 340269-63-8 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monomethanesulfonate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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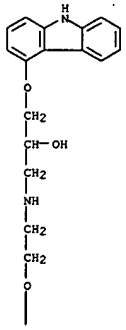

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CM 2

CRN 75-75-2
CMF C H4 O3 S

RN 374779-41-6 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrochloride (9CI) (CA INDEX NAME)

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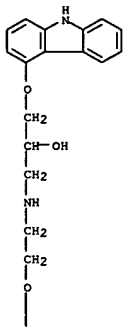

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● HCl

RN 787598-89-4 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
ethanedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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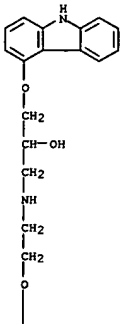

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CM 2

CRN 144-62-7
CMF C2 H2 O4

RN 852995-90-5 CAPLUS
CN 2-Propanol,
1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,
monohydrobromide, compd. with ethanol (9CI) (CA INDEX NAME)

CM 1

CRN 72956-09-3
CMF C24 H26 N2 O4

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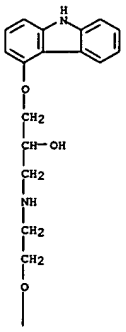

L5 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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CM 2

CRN 64-17-5
CMF C2 H6 O

L5 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:371418 CAPLUS
DOCUMENT NUMBER: 142:404218
TITLE: Pharmacokinetics- and genotyping-based systems and methods for optimizing drug therapy
INVENTOR(S): Heinrich, Gunther; Roots, Ivar
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005038049	A2	20050428	WO 2004-EP11180	20041006
WO 2005038049	A3	20060302		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-22604 A 20031006

AB Systems and the use of genotyping in the individualization of therapy and/or individualization of drug dosing are provided. More specifically, a pharmacokinetic model is described for the individualization of drug therapy.
IT 72956-09-3, Carvedilol
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacokinetics- and genotyping-based systems and methods for optimizing drug therapy)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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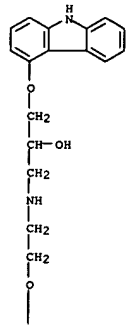

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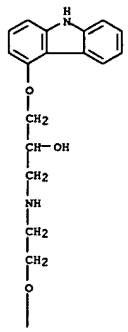
L5 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:288659 CAPLUS
DOCUMENT NUMBER: 142:456654
TITLE: Association between beta-1 and beta-2 adrenergic receptor gene polymorphisms and the response to beta-blockade in patients with stable congestive heart failure
AUTHOR(S): De Groote, Pascal; Helbecque, Nicole; Lamblin, Nicolas; Hermant, Xavier; Mc Fadden, Eugene; Foucher-Hossein, Claude; Amouyel, Philippe; Dallongeville, Jean; Bauters, Christophe
CORPORATE SOURCE: Service de Cardiologie C, Hopital Cardiologique, Centre Hospitalier, Universitaire de Lille, Lille, Fr.
SOURCE: Pharmacogenetics and Genomics (2005), 15(3), 137-142
CODEN: PGHEAI
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have clearly demonstrated the beneficial effect of β-blockers in patients with stable congestive heart failure (CHF). β-Blockers improve left ventricular ejection fraction (LVEF) and reduce cardiac mortality. However, there is an interindividual variability in the response to these agents. Two studies have suggested a possible impact of some functional βAR gene polymorphisms on the effects of β-blockade. The objective of the study is to analyze the association between genetic variations in the β1 or the β2 adrenoreceptor (AR) gene and the effects of β-blockade in patients with stable CHF. We studied 199 consecutive patients with stable CHF not treated with β-blockers. Before introduction of β-blockers and 3 mo after the maximal tolerated dose was reached, patients underwent an echocardiog. and a radionuclide angiog. The β1ARGly389Arg, β1ARSer49Gly, β2ARGly16Arg, β2ARGln27Glu and β2ARThr164Ile polymorphisms were determined: β-blockade resulted in a significant decrease in heart rate, a significant increase in LVEF (from 30±10% to 40±13%, P<0.0001). There was no association between the five polymorphisms and heart rate or LVEF, either before or after β-blockade. Heart rate and LVEF responses to β-blockade were not associated with the β1AR or the β2AR polymorphisms. βAR polymorphisms did not explain the interindividual variability in the response to β-blockers.
IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(βAR polymorphisms and beta-blockade response in patients with congestive heart failure)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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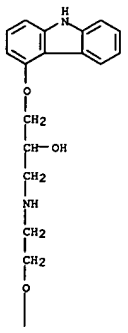
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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L5 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259810 CAPLUS
DOCUMENT NUMBER: 142:310909
TITLE: Detection of β-adrenergic receptor polymorphisms for risk assessment, survival prediction and treatment of heart failure
INVENTOR(S): Liggett, Stephen Bryant; Wagoner, Lynne Elizabeth
PATENT ASSIGNEE(S): University of Cincinnati, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005025409	A2	20050324	WO 2004-US29838	20040913
WO 2005025409	A3	20051208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004272102	A1	20050324	AU 2004-272102	20040913
CA 2538222	AA	20050324	CA 2004-2538222	20040913
US 2005112632	A1	20050526	US 2004-941063	20040913
EP 1670954	A2	20060621	EP 2004-816181	20040913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-502837P	P 20030912
			WO 2004-US29838	W 20040913

AB The invention relates to methods of detection of polymorphisms in β1-adrenergic receptor gene for diagnosis and prevention of cardiac conditions. The Gly389 β1-adrenergic receptor variants are not as responsive to treatment β blockers such as carvedilol, metoprolol or bisoprol. Thus, genotyping β1-adrenergic receptor polymorphisms is useful for predicting relative responsiveness to treatment with beta blockers. The Gly389 polymorphism also may be used, alone or in conjunction with other adrenergic receptor polymorphisms, to predict relative risk of developing cardiovascular diseases such as heart failure or to predict relative survival rate in patients with heart failure or other cardiovascular diseases. Also provided are transgenic mice and transgenic cells expressing the β1-adrenergic receptor polymorphisms, and their use in identifying therapeutic agents.

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β blocker therapy; detection of β-adrenergic receptor polymorphisms for risk assessment, survival prediction and treatment of heart failure)

RN 72956-09-3 CAPLUS

L5 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:158019 CAPLUS
DOCUMENT NUMBER: 142:456975
TITLE: Inhibition of chemiluminescence by carvedilol in the cell-free system, whole human blood and blood cells
AUTHOR(S): Nosal', R.; Jancinova, V.; Ciz, M.; Drabikova, K.; Lojek, A.; Fabryova, V.
CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (2005), 65(1), 55-64
CODEN: SJCLAY; ISSN: 0036-5513
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carvedilol inhibits luminol-enhanced chemiluminescence of reactive oxygen metabolites in vitro. In this study it was found that, in the cell-free system, carvedilol dose-dependently decreased chemiluminescence in the following ranking order of radicals: hydroxyl radical>hydrogen peroxide>superoxide radical. The inhibition of myeloperoxidase was significant with carvedilol concns. of 10 and 100 μmol/l and manifested in the concentration-dependent shift of chemiluminescence peaks to the right. In whole blood, carvedilol in concns. of 10 and 100 μmol/l significantly inhibited chemiluminescence induced by both receptor-bypassing stimuli (A23187, PMA) and receptor-operating stimuli (fMLP, OpZ). Carvedilol dose-dependently inhibited chemiluminescence of isolated human polymorphonuclear leukocytes in the ranking order of stimuli: A23187>OpZ>fMLP. In the presence of blood platelets, carvedilol did not substantially change chemiluminescence induced by fMLP and OpZ, while it was much more effective on chemiluminescence stimulated with calcium ionophore A23187. This could be the result of the supportive effect of serotonin liberated from platelets by A23187.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol dose-dependently decreased CL of reactive oxygen metabolite generated in cell free system, inhibited CL induced by A23187, PMA, fMLP, OpZ in human blood, PMNL and CL induced by A23187 in PMNL in presence of blood platelets)

RN 72956-09-3 CAPLUS

CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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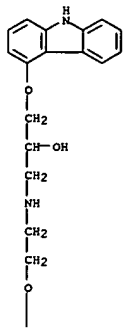

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REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

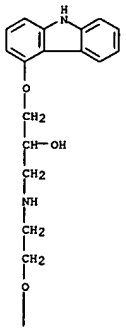
ACCESSION NUMBER: 2004:515723 CAPLUS
DOCUMENT NUMBER: 141:48620
TITLE: Polymorphisms in α2B adrenoreceptor gene associated with increased risk for type-2 diabetes or a metabolic syndrome and methods for diagnosis and treatment
INVENTOR(S): Salonen, Jukka T.; Pirskanen, Mia; Tuomainen, Tomi-Pekka; Yunus, Faisel
PATENT ASSIGNEE(S): Oy Jurilab Ltd, Finland
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004053158	A1	20040624	WO 2003-FI946	20031211
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
FI 2002002178	A	20040612	FI 2002-2178	20021211
AU 2003285382	A1	20040630	AU 2003-285382	20031211
EP 1570076	A1	20050907	EP 2003-778370	20031211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE, HU				
US 2006154249	A1	20060713	US 2006-538198	20060106
PRIORITY APPLN. INFO.:			FI 2002-2178 A	20021211
			WO 2003-FI946 W	20031211

AB The present invention provides methods for detecting polymorphisms in α2B adrenoreceptor gene associated with increased risk for diabetes or metabolic syndrome and diagnostic and therapeutic applications. The presence of the variant genotype indicates an increased risk of diabetes or a metabolic syndrome in said subject. The invention also relates to a method for the treatment of type 2 diabetes.
IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polymorphisms in α2B adrenoreceptor gene associated with increased risk for diabetes or metabolic syndrome and methods for diagnosis and treatment)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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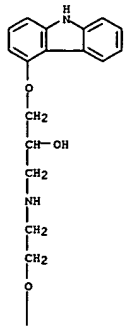
L5 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:418971 CAPLUS
DOCUMENT NUMBER: 141:47707
TITLE: Markedly reduced effects of (-)-isoprenaline but not of (-)-CGP12177 and unchanged affinity of β-blockers at Gly389-β1-adrenoceptors compared to Arg389-β1-adrenoceptors
AUTHOR(S): Joseph, S. S.; Lynham, J. A.; Grace, A. A.; Colledge, W. H.; Kaumann, A. J.
CORPORATE SOURCE: Department of Physiology, University of Cambridge, Cambridge, CB2 3EG, UK
SOURCE: British Journal of Pharmacology (2004), 142(1), 51-56
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Substitution of arginine by glycine at position 389, a frequent β1-adrenoceptor polymorphism, reduces adenylyl cyclase stimulation by (-)-isoprenaline. β1-Adrenoceptors mediate the effects of catecholamines and nonconventional partial agonists ((-)-CGP12177) through different sites. The authors investigated the influence of the 389 polymorphism on β blocker affinity, as well as on the responses to (-)-isoprenaline and the nonconventional partial agonist (-)-CGP12177 on cAMP levels in CHO cells expressing recombinant Arg 389-β1-adrenoceptors (101 fmol mg-1 protein) or Gly 389-β1-adrenoceptors (94 fmol mg-1). The affinity of β-blockers and partial agonists, estimated from competition binding with (-)-[125I]-cyanopindolol, was not different for Arg 389-β1-adrenoceptors and Gly 389-β1-adrenoceptors. The maximum cAMP increases by (-)-isoprenaline and (-)-CGP12177 at Gly 389-β1-adrenoceptors were reduced by 97 and 46%, but the potencies enhanced 2 and 0.5 log units, resp., compared to Arg 389-β1-adrenoceptors. The intrinsic activity of (-)-CGP12177 with respect to the (-)-isoprenaline was 0.057 at Arg 389-β1-adrenoceptors and 1.05 at Gly 389-β1-adrenoceptors. The authors confirm in intact CHO cells that responses to (-)-isoprenaline are markedly reduced at Gly 389-β1-adrenoceptors compared to Arg 389-β1-adrenoceptors. However, the 389 polymorphism reduces considerably less the agonist responses to (-)-CGP12177, indicating that coupling to Gs protein is different for β1-adrenoceptors activated by catecholamines than for receptors activated by nonconventional partial agonists. The affinity of β-blockers is conserved across the Arg389Gly polymorphism.
IT 72956-09-3, (±)-Carvedilol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β1-adrenoceptors polymorphism effect on signaling response to isoprenaline and partial agonist CGP12177 and affinity of β-blockers)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:243504 CAPLUS
DOCUMENT NUMBER: 141:288791
TITLE: Effects of carvedilol on oxidative stress in polymorphonuclear and mononuclear cells in patients with essential hypertension
AUTHOR(S): Yasunari, Kenichi; Maeda, Kensaku; Nakamura, Munehiro; Watanabe, Takanori; Yoshikawa, Junichi; Asada, Akira
CORPORATE SOURCE: Graduate School of Medicine, Department of General Medicine and Cardiology, Osaka City University, Osaka, Japan
SOURCE: American Journal of Medicine (2004), 116(7), 460-465
CODEN: AJMEAZ; ISSN: 0002-9343
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

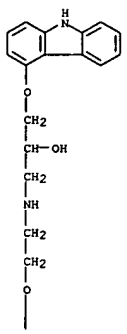
AB Purpose: To compare the effects of carvedilol and propranolol on oxidative stress in leukocytes and C-reactive protein levels in patients with hypertension. Methods: Sixty hypertensive patients were randomly assigned to carvedilol (20 mg; n = 30) or propranolol (60 mg; n = 30) for 6 mo. Thirty normotensive subjects who were given placebo served as controls. Oxidative stress in polymorphonuclear cells and mononuclear cells were measured by gated flow cytometry. C-reactive protein levels were measured by immunonephelometric assay. Results: Oxidative stress in polymorphonuclear cells and mononuclear cells was increased significantly in hypertensive patients compared with in normotensive controls. After 6 mo of treatment, carvedilol decreased oxidative stress significantly in polymorphonuclear cells by a mean of 45 arbitrary units (95% confidence interval [CI]: 32 to 59 arbitrary units; P <0.001) and propranolol decreased oxidative stress significantly by 20 arbitrary units (95% CI: 7 to 33 arbitrary units; P <0.003; P = 0.001 for difference between treatments). Carvedilol also decreased oxidative stress significantly in mononuclear cells by 23 arbitrary units (95% CI: 15 to 31 arbitrary units; P <0.001), whereas propranolol decreased oxidative stress by 2 arbitrary units (95% CI: 7 to 12 arbitrary units; P = 0.62; P = 0.002 for difference between treatments). Carvedilol decreased C-reactive protein levels significantly by a median of 0.073 mg/dL (interquartile range, 0.034 to 0.112 mg/dL; P <0.001), whereas propranolol decreased levels by 0.012 mg/dL (interquartile range, 0.009 to 0.032 mg/dL; P = 0.26; P = 0.003 for difference between treatments). Conclusion: These findings suggest that carvedilol inhibits oxidative stress in polymorphonuclear and mononuclear cells, as well as lowers C-reactive protein levels, to a greater extent than does propranolol in hypertensive patients.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol inhibited oxidative stress in polymorphonuclear and mononuclear cells and lowered C-reactive protein levels to greater extent than propranolol did in patient with essential hypertension)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

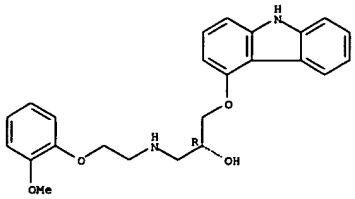
ACCESSION NUMBER: 2004:173488 CAPLUS
DOCUMENT NUMBER: 141:270928
TITLE: CYP2D6 genotype and induction of intestinal drug transporters by rifampin predict presystemic clearance of carvedilol in healthy subjects
AUTHOR(S): Giessmann, Thomas; Modess, Christiane; Hecker, Ute; Zschiesche, Michael; Dazert, Peter; Kunert-Keil, Christiane; Warzok, Rolf; Engel, Georg; Weitschies, Werner; Cascorbi, Ingolf; Kroemer, Heyo K.; Siegmund, Werner
CORPORATE SOURCE: Department of Clinical Pharmacology, Pharmacology, and Pharmacy, Peter Holtz Research Center of Pharmacology and Experimental Therapeutics, University of Greifswald, Greifswald, D-17487, Germany
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis, MO, United States) (2004), 75(3), 213-222
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background. Clin. trials have indicated that the combined β- and α-adrenergic receptor blocker carvedilol improves the survival rate in patients with advanced chronic heart failure. The objective of our study was the identification and quantification of factors that modulate steady-state serum concns. of carvedilol and its enantiomers and that may influence therapeutic efficacy and safety. Methods. The influence of genetic variants of cytochrome P 450 (CYP) 2D6 and CYP2C9 and of transporter proteins (P-glycoprotein, multidrug resistance protein 2 [MRP2]) on the disposition of carvedilol and its enantiomers after i.v. (5 mg) and long-term oral administration (25 mg for 7 days) was assessed in 12 healthy subjects. The intestinal expression of P-glycoprotein and MRP2 was analyzed by quant. real-time polymerase chain reaction and immunohistochem. techniques. Results. The area under the serum concentration-time curve (AUC) values of carvedilol were significantly (P < .05) increased in 6 subjects with CYP2D6 deficiency, with effects being more pronounced for R(+)-carvedilol (230 ± 72.6 ng · h/mL vs. 93.9 ± 64.6 ng · h/mL in extensive metabolizers) than for S(-)-carvedilol (62.9 ± 21.1 ng · h/mL vs. 32.7 ± 14.5 ng · h/mL). The AUC and fecal excretion of i.v. carvedilol were correlated with the intestinal expression of MDR1 mRNA (mRNA) (r = -0.67, P = .001; r = 0.83, P = .002) and MRP2 mRNA (r = -0.74, P < .001; r = 0.70, P = .025). Furthermore, we measured the disposition of long-term oral carvedilol after comedication of the pregnane X receptor ligand rifampin (INN, rifampicin) (600 mg, 9 days), which up-regulates both P-glycoprotein and MRP2 but not CYP2D6. Rifampin decreased the AUC of carvedilol to an extent independent of the CYP2D6 genotype (poor metabolizers, 341 ± 147 ng · h/mL vs. 126 ± 41.7 ng · h/mL; extensive metabolizers, 173 ± 102 ng · h/mL vs. 74 ± 41.4 ng · h/mL; both P < .05). The AUC was significantly correlated with intestinal expression of MDR1 mRNA (r = -0.671, P = .001) and MRP2 mRNA (r = -0.595, P < .006). Conclusions. Variable plasma concns. of carvedilol during long-term administration are predicted by CYP2D6 genotype and intestinal expression of P-glycoprotein and MRP2.

IT 95093-99-5, (+)-Carvedilol 95094-00-1, (-)-Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological

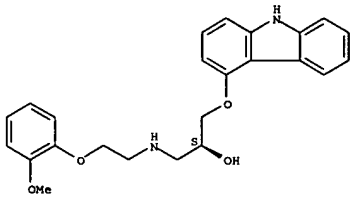
L5 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
study): USES (Uses)
(AUC of carvedilol were significantly increased in human with CYP2D6 deficiency with effects being more pronounced for R(+)-carvedilol rather than S(-)-carvedilol)
RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

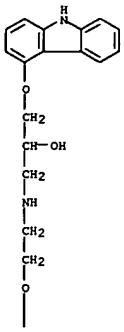
Absolute stereochemistry.



IT 72956-09-3, Carvedilol
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term administration of carvedilol showed variable plasma concentration
predicted by CYP2D6 genotype, intestinal expression of P-glycoprotein and MRP2 and may effect efficacy and safety of its therapeutic use in healthy human)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-

L5 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

PAGE 1-A



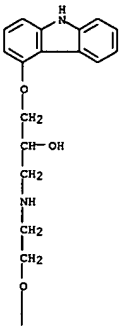
PAGE 2-A

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:145230 CAPLUS
DOCUMENT NUMBER: 141:218619
TITLE: Rationale and design of a large-scale trial using nicorandil as an adjunct to percutaneous coronary intervention for ST-segment elevation acute myocardial
infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damage by a K-ATP channel opener (J-WIND-KATP)
AUTHOR(S): Minamino, Tetsuo; Kim, Jiyoong; Asakura, Masanori; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi
CORPORATE SOURCE: J-WIND Investigators, Japan Foundation for Aging and Health for Medical Frontier Strategy Research by Health and Labor Sciences Research Grants, National Cardiovascular Center, Suita, Japan
SOURCE: Circulation Journal (2004), 68(2), 101-106
CODEN: CJIOBY; ISSN: 1346-9843
PUBLISHER: Japanese Circulation Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, nicorandil, a hybrid of an ATP-sensitive K+ (KATP) channel opener and nitrates, reduces infarct size, so the Japan-Working groups of acute myocardial Infarction for the reduction of Necrotic Damage by a K-ATP
channel opener (J-WIND-KATP) designed a prospective, randomized, multicenter study to evaluate whether nicorandil reduces myocardial infarct size and improves regional wall motion when used as an adjunctive therapy for AMI. Methods and Results: Twenty-six hospitals in Japan are participating in the J-WIND-KATP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. nicorandil or placebo. The primary end-points are (1) estimated infarct size
and (2) left ventricular function. Single nucleotide polymorphisms (SNPs) that may be associated with the function of KATP-channel and the susceptibility of AMI to the drug will be examined Furthermore, a data mining method will be used to design the optimal combined therapy for post-myocardial infarction (MI) patients. Conclusions: It is intended that J-WIND-KATP will provide important data on the effects of nicorandil as an adjunct to PCI for AMI and that the SNPs information that will open the field of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.
IT 72956-09-3, Carvedilol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nicorandil and cardiovascular agent for decreasing risk of cardiac events in patients with post-myocardial infarction)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:145229 CAPLUS
DOCUMENT NUMBER: 141:219275
TITLE: Rationale and design of a large-scale trial using atrial natriuretic peptide (ANP) as an adjunct to percutaneous coronary intervention for ST-segment elevation acute myocardial infarction: Japan-working groups of acute myocardial infarction for the reduction of necrotic damage by ANP (J-WIND-ANP)
AUTHOR(S): Asakura, Masanori; Kim, Jiyoong; Minamino, Tetsuo; Shintani, Yasunori; Asanuma, Hiroshi; Kitakaze, Masafumi
CORPORATE SOURCE: J-WIND Investigators, Japan Society for the Promotion of Science for Young Scientists, Osaka University Graduate School of Medicine, Suita, Japan
SOURCE: Circulation Journal (2004), 68(2), 95-100
CODEN: CJIOBY; ISSN: 1346-9843
PUBLISHER: Japanese Circulation Society
DOCUMENT TYPE: Journal
LANGUAGE: English

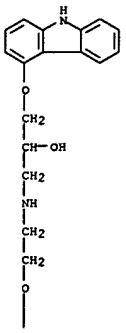
AB Background: The benefits of percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI) are limited by reperfusion injury. In animal models, atrial natriuretic peptide (ANP) reduces infarct size, so the Japan-Working groups of acute myocardial Infarction for the reduction of Necrotic Damage by ANP (J-WIND-ANP) designed a prospective, randomized, multicenter study, to evaluate whether ANP as an adjunctive therapy for AMI reduces myocardial infarct size and improves regional wall motion. Methods and Results: Twenty hospitals in Japan will participate in the J-WIND-ANP study. Patients with AMI who are candidates for PCI are randomly allocated to receive either i.v. ANP or placebo administration. The primary end-points are (1) estimated infarct size (Σ-creatine kinase and troponin T) and (2) left ventricular function (left ventriculograms). Single nucleotide polymorphisms (SNPs) that may be associated with the function of ANP and susceptibility of AMI will be examined Furthermore, a data mining method will be used to design the optimal combinational therapy for post-MI patients. Conclusions: J-WIND-ANP will provide important data on the effects of ANP as an adjunct to PCI for AMI and the SNPs information will open the field of tailor-made therapy. The optimal therapeutic drug combination will also be determined for post-MI patients.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug therapy for data mining of cardiovascular therapy combination; large-scale trial rationale and design using atrial natriuretic peptide (ANP) as adjunct to PCI for ST-segment elevation acute myocardial infarction patients)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:96877 CAPLUS
DOCUMENT NUMBER: 141:184845
TITLE: Beta-adrenergic receptor blockade and the angiotensin-converting enzyme deletion polymorphism in patients with chronic heart failure
AUTHOR(S): De Groote, Pascal; Helbecque, Nicole; Lamblin, Nicolas; Hermant, Xavier; Amouyel, Philippe; Bauters, Christophe; Dallongeville, Jean
CORPORATE SOURCE: Hopital Cardiologique, Service de Cardiologie C, Centre Hospitalier Universitaire de Lille, Lille, 59037, Fr.
SOURCE: European Journal of Heart Failure (2004), 6(1), 17-21
CODEN: EJHFFS; ISSN: 1388-9842
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Beta-adrenergic receptor blockade is an established treatment of chronic heart failure (HF). Previous studies have suggested a potential pharmacogenetic interaction between beta-blocker therapy and the angiotensin-converting enzyme (ACE) I/D polymorphism in patients with HF. Aims: We designed this study to analyze changes in myocardial function of HF patients in response to beta-blocker therapy as a function of the ACE I/D polymorphism. Methods and results: We studied 199 consecutive patients with chronic HF not treated with beta-blockers. Before initiation of beta-blockers and 3 mo after the maximal tolerated dose was reached, patients underwent echocardiog., radionuclide angiog., and a cardiopulmonary exercise test. We extracted genomic DNA from white blood cells and determined the ACE I/D polymorphism. Thirty-five (18%) patients had the II genotype, 86 (43%) the ID genotype and 78 (39%) the DD genotype. A significant and similar improvement in left ventricular ejection fraction (LVEF) was observed in II (from 0.30±0.10 to 0.41±0.13; P<0.0001), ID (from 0.29±0.11 to 0.39±0.13; P<0.0001) and DD patients (from 0.31±0.11 to 0.40±0.13; P<0.0001). Peak Vo2 before and after beta-blockade was similar among the three groups. The proportion of responders to beta-blockers (patients without cardiac events during titration who had an increase in LVEF >5% after beta-blockers) was similar among the three groups (II: 65.9%, ID: 60.6%, DD: 65.9%; P=NS). During a median follow-up of 933 days, there was no evidence for any effect of ACE I/D polymorphism on cardiac survival. Conclusions: We observed no evidence of pharmacogenetic interaction between the ACE I/D polymorphism and the effects of beta-blockade on LVEF and other prognostic parameters in patients with chronic HF. Our results support the initiation of beta-blockers in HF patients with the II or the ID genotype as well as in those with the DD genotype.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE I/D, ACE DD and ACE II genotype showed similar changes in LVEF, LVEDD, survival rate, Vo2 in chronic HF patient treated with beta blockers carvedilol and bisoprolol suggesting no interaction between ACE I/D and beta blocker treatment)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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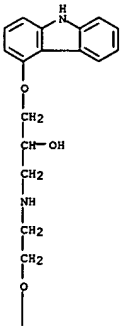

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REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:570906 CAPLUS
DOCUMENT NUMBER: 139:122716
TITLE: Crystalline solids of carvedilol and processes for their preparation
INVENTOR(S): Kor, Ilan; Wizel, Shlomit
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003059807	A2	20030724	WO 2003-US1137	20030115
WO 2003059807	A3	20031204		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2472377	AA	20030724	CA 2003-2472377	20030115
AU 2003205146	A1	20030730	AU 2003-205146	20030115
US 2003166702	A1	20030904	US 2003-342905	20030115
US 6710184	B2	20040323		
EP 1474133	A2	20041110	EP 2003-703815	20030115
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1615133	A	20050511	CN 2003-802210	20030115
JP 2005515226	T2	20050526	JP 2003-559922	20030115
US 2004171665	A1	20040902	US 2003-712799	20031112
ZA 2004005443	A	20050708	ZA 2004-5443	20040708
NO 2004003383	A	20040813	NO 2004-3383	20040813

PRIORITY APPLN. INFO.: US 2002-349310P P 20020115
US 2003-342905 A3 20030115
WO 2003-US1137 W 20030115

AB This invention relates to a novel crystalline solid of carvedilol or a solvate thereof, to processes for its preparation, to compns. containing it and to its use in medicine. This invention further relates to a novel process for preparing a crystalline solid of carvedilol form II.

IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(crystalline solids of carvedilol and processes for their preparation)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-

L5 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(9CI) (CA INDEX NAME)

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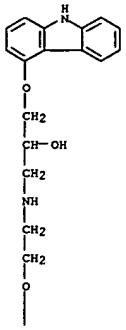


PAGE 2-A

L5 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:516046 CAPLUS
DOCUMENT NUMBER: 140:104792
TITLE: β-Adrenoceptor genotype influences the response to carvedilol in patients with congestive heart failure
AUTHOR(S): Kaye, David M.; Smirk, Belinda; Williams, Carolyn; Jennings, Garry; Esler, Murray; Holst, Dianne
CORPORATE SOURCE: Heart Centre, Alfred Hospital and Baker Medical Research Institute, Melbourne, Australia
SOURCE: Pharmacogenetics (2003), 13(7), 379-382
CODEN: PHMCEE; ISSN: 0960-314X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

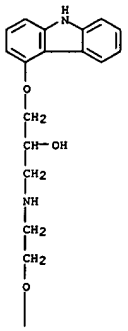
AB Although the widespread introduction of β-adrenoceptor antagonists into the management of congestive heart failure (CHF) has led to significant improvements in morbidity and mortality, it is also apparent that clin. responses to this therapy vary substantially. With the recognition that functionally significant genetic polymorphisms of the β2-adrenoceptor exist with clin. relevant allelic frequency, the authors hypothesized that β2-adrenoceptor genotype may affect the response to carvedilol. The clin. response, influence on left ventricular function and β2-adrenoceptor (β2AR) genotype was determined in 80 patients treated with carvedilol. A clin. significant improvement in left ventricular function (good responder) was defined as an absolute improvement of 10% in the left ventricular ejection fraction or 5% in the fractional shortening. Consistent with studies performed in vitro on the influence of β2AR genotype and receptor desensitization, subjects who were homozygous for the allele encoding the Gln 27 polymorphism displayed a significantly lower proportion of good responders than patients who were homozygous or heterozygous for the Glu 27 polymorphism (26% vs. 63%, P = 0.003). These data demonstrate a significant influence of β2AR genotype in the response to carvedilol in CHF patients. Accordingly, determination of β2AR status may be of value in the tailoring of individual therapy in patients with CHF.

IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(β-adrenoceptor genotype influences the response to carvedilol in humans with congestive heart failure)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-
(9CI) (CA INDEX NAME)

L5 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:282536 CAPLUS
DOCUMENT NUMBER: 138:292802
TITLE: Pseudopolymorphic forms of carvedilol
INVENTOR(S): Bubendorf, Andre Gerard; Gabel, Rolf-dieter; Henning, Michael; Krimmer, Siegfried; Neugebauer, Guenter; Preis, Walter; Wirl, Alexander
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029214	A1	20030410	WO 2002-EP10451	20020918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2460486	AA	20030410	CA 2002-2460486	20020918
EP 1432681	A1	20040630	EP 2002-777139	20020918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
BR 2002012927	A	20041013	BR 2002-12927	20020918
CN 1558900	A	20041229	CN 2002-818741	20020918
JP 2005507899	T2	20050324	JP 2003-532464	20020918
US 2003119893	A1	20030626	US 2002-255290	20020926
US 2004198812	A1	20041007	US 2004-827859	20040420
US 2006148878	A1	20060706	US 2006-325754	20060105

PRIORITY APPLN. INFO.:
EP 2001-123422 A 20010928
WO 2002-EP10451 W 20020918
US 2002-255290 B1 20020926
US 2004-827859 B1 20040420

AB The present invention is related to pseudopolymorphic forms of 1-(4-carbazolyloxy)-3[2-(2-methoxyphenoxy)ethylamino]-2-propanol (carvedilol) or its optically active forms or pharmaceutically acceptable salts, processes for their preparation, and pharmaceutical compns. containing them for the treatment or prophylaxis of cardiac diseases.

IT 507239-85-2
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pseudopolymorphic forms of carvedilol for modified-release dosage forms for treatment of cardiac diseases)

RN 507239-85-2 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-,

L5 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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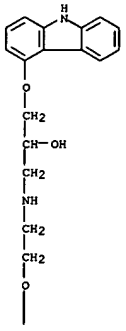
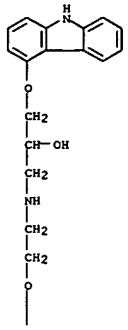


PAGE 2-A

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
hydrate (2:1) (9CI) (CA INDEX NAME)

PAGE 1-A



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●1/2 H_2O

IT 72956-09-3, Carvedilol
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of pseudopolymorphic forms of carvedilol for modified-release dosage forms for treatment of cardiac diseases)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:242149 CAPLUS
DOCUMENT NUMBER: 138:276256
TITLE: Controlled release pharmaceutical compositions containing polymers
INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Lademann, Anne-Marie; Jensen, Christine
PATENT ASSIGNEE(S): Egalet A/S, Den.
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

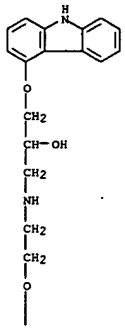
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024429	A1	20030327	WO 2002-DK620	20020923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429739	A1	20040623	EP 2002-779224	20020923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2004234602	A1	20041125	US 2004-490308	20040623

PRIORITY APPLN. INFO.:
DK 2001-1377 A 20010921
DK 2002-1044 A 20020703
WO 2002-DK620 W 20020923

AB A method for controlling the release of at least one therapeutically, prophylactically and/or diagnostically active substance into an aqueous medium by erosion of at least one surface of a pharmaceutical composition The method comprises adjusting the concentration and/or the nature of the ingredients making up the matrix composition in such a manner so as to obtain an approx. zero-order release of the drug from the pharmaceutical composition when subject to an in vitro dissoln. test as described herein. The composition comprises a matrix composition containing a polymer or a mixture of polymers that may be substantially water soluble and/or crystalline, an active substance and, optionally, one or more pharmaceutically acceptable excipients, and a coating. Typical polymers are PEG. The coating comprises a first cellulose derivative which is substantially insol. in the aqueous medium, and at least one of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and a filler. The active ingredient may be carvedilol. Stable solid dispersions of active substances having low

L5 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
water soly. are also disclosed. Thus, a compn. contained PEG 64.6, carvedilol 30, and citric acid 5.4% by wt.
IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release pharmaceutical compns. containing polymers)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

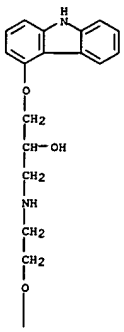
L5 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:242148 CAPLUS
DOCUMENT NUMBER: 138:276255
TITLE: Controlled release solid dispersions containing carvedilol
INVENTOR(S): Fischer, Gina; Bar-Shalom, Daniel; Slot, Lillian; Lademann, Anne-Marie; Jensen, Christine
PATENT ASSIGNEE(S): Egalet A/S, Den.
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024426	A1	20030327	WO 2002-DK621	20020923
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1429734	A1	20040623	EP 2002-776907	20020923
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
US 2005019399	A1	20050127	US 2004-490170	20040921
PRIORITY APPLN. INFO.:			DK 2001-1375 A	20010921
			DK 2001-1611 A	20011031
			DK 2002-1044 A	20020703
			WO 2002-DK621 W	20020923

AB A controlled release pharmaceutical composition for oral use comprises a solid dispersion of at least one therapeutical agent and/or diagnostic substance, which at least partially is in an amorphous form, a polymer that has plasticizing properties, and optionally, a stabilizing agent, the at least one active substance having a limited water solubility, and the composition being designed to release the active substance with a substantially zero order release. The polymer is typically a polyethylene glycol and/or polyethylene oxide having a mol. weight of at least about 20,000 in crystalline and/or amorphous form or a mixture of such polymers, and the active substance is typically carvedilol. The composition may comprise a coated matrix, the coating comprising a first cellulose derivative which is substantially insol. in the aqueous medium, and at least one of a second cellulose derivative which is soluble or dispersible in water, a plasticizer, and a filler. Thus, a composition contained PEG 64.6, carvedilol 30, and citric acid 5.4% by weight The dissoln. profile corresponded to a zero-order

L5 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
release of carvedilol from the compn.
IT 72956-09-3, Carvedilol
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release solid dispersions containing carvedilol)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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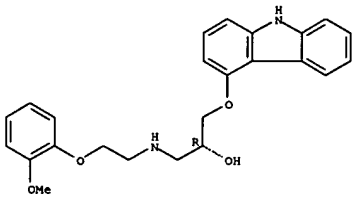
IT 95093-99-5 95094-00-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled release solid dispersions containing carvedilol)
RN 95093-99-5 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2R)- (9CI) (CA INDEX NAME)

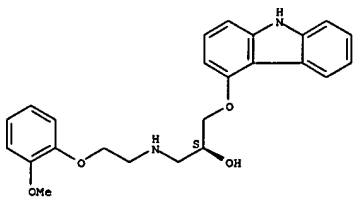
Absolute stereochemistry.

L5 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 95094-00-1 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:57865 CAPLUS
DOCUMENT NUMBER: 138:126962
TITLE: Carvedilol polymorph
INVENTOR(S): Chen, Wei; Gallop, Marc; Oh, Choon K.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003005970	A2	20030123	WO 2002-US22374	20020715
WO 2003005970	A3	20030501		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1406614	A2	20040414	EP 2002-761099	20020715
EP 1406614	B1	20060607		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2004534840	T2	20041118	JP 2003-511779	20020715
AT 328595	E	20060615	AT 2002-761099	20020715
US 2004152756	A1	20040805	US 2004-483217	20040108

PRIORITY APPLN. INFO.: US 2001-305593P P 20010713
US 2001-314150P P 20010822
WO 2002-US22374 W 20020715

AB This invention relates to a crystalline form of carvedilol (Form III), and to the use of pharmaceutical compns. containing carvedilol Form III for treatment of hypertension, angina, or congestive heart failure. The carvedilol Form III was prepared from carvedilol Form II.

IT 72956-09-3, Carvedilol
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation and properties of carvedilol polymorph)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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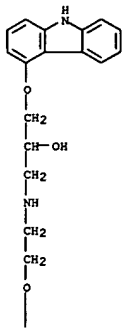

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L5 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:871259 CAPLUS
DOCUMENT NUMBER: 139:17321
TITLE: Activated polymorphonuclear leukocytes induce cardiomyocyte apoptosis and the protective effects of carvedilol
AUTHOR(S): Dun, Y.; Zhi, J.-M.; Sun, H.-Y.; Zhao, R.-R.; Zhao, Z.-Q.
CORPORATE SOURCE: Laboratory of Cardiovascular Physiology, Shanxi Medical University, Taiyuan, Peop. Rep. China
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (2002), 24(7), 403-412
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous studies have shown that ischemia and reperfusion are potent stimuli for eliciting cardiomyocyte apoptosis, and that polymorphonuclear leukocytes (PMNs) are involved in the development of myocardial injury induced by ischemia and reperfusion. The present study examined whether PMN could directly induce cardiomyocyte apoptosis and, if so, its possible signal transduction pathways. In addition, we also investigated the effects of carvedilol, a potent antioxidant, on PMN-induced apoptosis. Cultured primary neonatal rat cardiomyocytes were exposed to PAF-activated PMNs at concns. of 105, 3 + 105 and 106 cells/well for 48 h. Multiple detecting techniques, including electron microscopy. DNA gel electrophoresis, TUNEL assay and flow cytometry were used to identify myocyte apoptosis. All of these techniques demonstrated that activated PMNs directly induced cardiomyocyte apoptosis in a concentration-dependent manner, while unactivated PMNs showed no such effect. Activated PMN-induced apoptosis was partially inhibited by SB203580, a specific inhibitor of the p38-MAPK signaling system. Carvedilol (at a dose range of 1-10 μmol/L) significantly prevented activated PMN-induced cardiomyocyte apoptosis. These results suggest that PMNs, when activated, directly induce cardiomyocyte apoptosis and that the p38-MAPK signaling pathway might be involved in this process. Carvedilol may prevent PMN-induced apoptosis possibly because of its antioxidant properties.

IT 72956-09-3, Carvedilol
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(activated polymorphonuclear leukocytes induce cardiomyocyte apoptosis and the protective effects of carvedilol)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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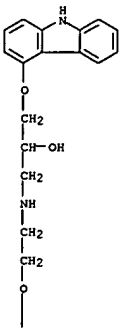

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REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:10275 CAPLUS
DOCUMENT NUMBER: 136:90914
TITLE: Preparation of carvedilol and its crystalline hydrate and solvate
INVENTOR(S): Hildesheim, Jean; Finogueev, Sergey; Aronhime, Judith; Dolitzky, Ben-Zion; Ben-Valid, Shoshana; Kor, Ilan
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000216	A1	20020103	WO 2001-US20760	20010628
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2413702	AA	20020103	CA 2001-2413702	20010628
US 2002143045	A1	20021003	US 2001-894798	20010628
US 6699997	B2	20040302		
EP 1299101	A1	20030409	EP 2001-950671	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004501191	T2	20040115	JP 2002-504998	20010628
CN 1733727	A	20060215	CN 2005-10086095	20010628
EP 1655285	A1	20060510	EP 2005-21195	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
ZA 2002010282	A	20031219	ZA 2002-10282	20021219
US 2004152757	A1	20040805	US 2004-758025	20040116
US 7056942	B2	20060606		
US 2004225132	A1	20041111	US 2004-758026	20040116
US 2006030614	A1	20060209	US 2005-217643	20050831

PRIORITY APPLN. INFO.:

US 2000-214356P	P	20000628
US 2000-246358P	P	20001107
CN 2001-814616	A3	20010628
EP 2001-950671	A3	20010628
US 2001-894798	A3	20010628
WO 2001-US20760	W	20010628
US 2004-758025	A3	20040116

AB This invention relates to an improved process of preparing carvedilol, as well as a new crystalline hydrate and solvate and forms of carvedilol,

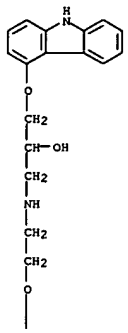
L5 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

processes for the manuf. thereof, and pharmaceutical compns. thereof. Carvedilol was prepd. by the reaction of 2-(2-methoxyphenoxy)ethylamine and 4-(oxiran-2-ylmethoxy)-9H-carbazole. Cryst. carvedilol form II was prepd. by crystg. carvedilol from isoamyl alc.

IT 72956-09-3P, Carvedilol 385765-36-6P
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of carvedilol and its crystalline hydrate and solvate)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

PAGE 1-A



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RN 385765-36-6 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-, hydrochloride, hydrate (9CI) (CA INDEX NAME)

L5 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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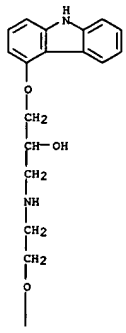

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●x HCl

●x H_2O

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L5 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:311764 CAPLUS
DOCUMENT NUMBER: 135:220998
TITLE: Pharmacogenetic interactions between β-blocker therapy and the angiotensin-converting enzyme deletion polymorphism in patients with congestive heart failure
AUTHOR(S): McNamara, Dennis M.; Holubkov, Richard; Janosko, Karen; Palmer, Amy; Wang, Jue J.; MacGowan, Guy A.; Murali, Srinivas; Rosenblum, Warren D.; London, Barry; Feldman, Arthur M.
CORPORATE SOURCE: Cardiovascular Institute, University of Pittsburgh Medical Center, Pittsburgh, PA, 15213, USA
SOURCE: Circulation (2001), 103(12), 1644-1648
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

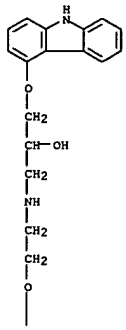
AB Activation of the renin-angiotensin and sympathetic nervous systems adversely affect heart failure progression. The ACE deletion allele (ACE D) is associated with increased renin-angiotensin activation; however, its influence on patient outcomes remains uncertain, and the pharmacogenetic interactions with β-blocker therapy have not been previously evaluated. We prospectively followed 328 patients (age, 56.1±11.9 yr) with systolic dysfunction (left ventricular ejection fraction, 0.24±0.08) to assess the impact of the ACE D allele on transplant-free survival (median follow-up, 21 mo). Transplant-free survival was compared by genotype for the whole cohort and sep. in patients with (n=120) and those without β-blocker therapy (n=208) at the time of entry. Transplant-free survival was significantly poorer for patients with the D allele (1-yr percent survival II/ID/DD=94/77/75; 2-yr=78/65/60; ordered log-rank test, P=0.044). In patients not treated with β-blockers, the adverse impact of ACE D allele was dramatically increased (1-yr percent survival II/ID/DD=95/75/67; 2-yr=81/61/48; P=0.005). In contrast, in patients receiving β-blocker therapy, no influence of ACE genotype on transplant-free survival was evident (1-yr percent survival II/ID/DD=91/80/86; 2-yr=70/71/77; P=0.73). In a cohort of patients with systolic dysfunction, the ACE D allele was associated with a significantly poorer transplant-free survival. This effect was primarily evident in patients not treated with β-blockers and was not seen in patients receiving therapy. These findings suggest a potential pharmacogenetic interaction between the ACE D/I polymorphism and therapy with β-blockers in the determination of heart failure survival.

IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacogenetic interactions between β-blocker therapy and angiotensin-converting enzyme deletion polymorphism in humans with congestive heart failure)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

L5 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

PAGE 1-A



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REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:127282 CAPLUS
DOCUMENT NUMBER: 132:288739
TITLE: No effect of carvedilol on nitric oxide generation in phagocytes but modulation of production of superoxide ions
AUTHOR(S): Asbrink, S.; Zickert, A.; Bratt, J.; Gyllenhammar, H.; Palmblad, J.
CORPORATE SOURCE: Clinical Research Center, The Center for Inflammation and Hematology Research, Departments of Medicine, Hematology, and Rheumatology, Huddinge University Hospital, Huddinge, S-141 86, Swed.
SOURCE: Biochemical Pharmacology (2000), 59(8), 1007-1013
CODEN: BCPCA6; ISSN: 0006-2952
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Since carvedilol has been claimed to possess antioxidative effects, this drug might affect functional responses, including nitric oxide (NO) generation, of polymorphonuclear neutrophils (PMN) and macrophages. When we assessed the effects of carvedilol on PMN responses in vitro, we observed that carvedilol dose dependently modulated generation of superoxide ions by NADPH oxidase when induced by the formylpeptide formyl-methionyl-leucyl-phenylalanine (fMLP) or the phorbol ester phorbol myristate acetate. This effect was not coupled to diminished phospholipase C activity. In contrast to the effect on NADPH oxidase, neither the fMLP-elicited NO generation by PMN nor the response of the murine macrophage cell line J774 to lipopolysaccharide was affected. There was no evidence from cell-free assay systems that carvedilol is a scavenger for superoxide ions or NO. Moreover, carvedilol did not affect other reactions dependent on NO, e.g. spontaneous or fMLP-stimulated PMN migration or lipoxin A4-, fMLP-, or A23187-induced neutrophil cytotoxicity for human umbilical vein endothelial cells. Thus, these effects point to the possibility that carvedilol modulates the NADPH oxidase of PMN but leaves the nitric oxide synthase of phagocytes intact.
IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(carvedilol does not affect nitric oxide generation in phagocytes but modulates superoxide ion production)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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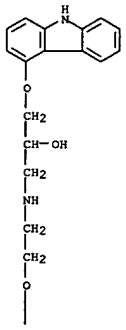

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REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:91653 CAPLUS
DOCUMENT NUMBER: 133:733
TITLE: Carvedilol inhibits reactive oxygen species generation by leukocytes and oxidative damage to amino acids
AUTHOR(S): Dandona, Paresh; Karne, Rajaram; Ghanim, Husam; Hamouda, Wael; Aljada, Ahmad; Magsino, Cesar H., Jr.
CORPORATE SOURCE: Division of Endocrinology, Diabetes, and Metabolism, State University of New York at Buffalo and Kaleida Health, Buffalo, NY, 14209, USA
SOURCE: Circulation (2000), 101(2), 122-124
CODEN: CIRCAZ; ISSN: 0009-7322
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to test whether carvedilol has an antioxidant effect in humans in vivo. We administered 3.125 mg of carvedilol twice daily to normal subjects for 1 wk. ROS generation by polymorphonuclear leukocytes and mononuclear cells fell from 314±183.43 and 303±116 mV to 185±157 and 189±63 mV (P<0.025), resp. M-Tyrosine fell from 4.24±0.99 to 4.03±0.97 ng/mL (P=0.01), and o-tyrosine fell from 4.59±1.10 to 4.24±0.99 ng/mL (P=0.004) in the absence of a change in phenylalanine concns. We conclude that carvedilol significantly inhibits ROS generation by leukocytes and oxidative conversion of phenylalanine to m- and o-tyrosine.
IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol inhibits reactive oxygen species generation by leukocytes and oxidative damage to amino acids)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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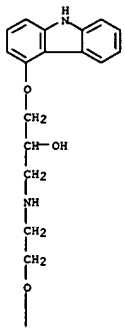

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REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:804673 CAPLUS
DOCUMENT NUMBER: 128:110226
TITLE: Pharmacology of carvedilol: rationale for use in hypertension, coronary artery disease, and congestive heart failure
AUTHOR(S): Ruffolo, Robert R., Jr.; Feuerstein, Giora Z.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406-0939, USA
SOURCE: Cardiovascular Drugs and Therapy (1997), 11(Suppl. 1), 247-256
CODEN: CDTHET; ISSN: 0920-3206
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 77 refs. Carvedilol is a novel, multiple-action cardiovascular drug that is currently approved in many countries for the treatment of hypertension. The reduction in blood pressure produced by carvedilol results primarily from β-adrenoceptor blockade and vasodilation, the latter resulting from α1-adrenoceptor blockade. These actions, as well as several of the other activities of carvedilol, are associated with cardioprotection in animal models that occurs to a degree that is greater than that observed with other drugs. The multiple actions of carvedilol may also provide the underlying rationale for the use of the drug in the treatment of coronary artery disease and congestive heart failure. By virtue of being both a beta-blocker and a vasodilator, carvedilol significantly decreases myocardial work by reducing all three components of myocardial oxygen demand, namely, heart rate, contractility, and wall tension. The vasodilatory effects of carvedilol reduce afterload, and the resulting decrease in impedance to left ventricular ejection offsets the neg. inotropic effect that would normally result from beta-blockade. As a consequence, stroke volume and cardiac output are maintained or even increased in animals and in patients with congestive heart failure who are treated with carvedilol. Carvedilol and several of its metabolites are potent antioxidants, and this activity may account, in part, for the cardioprotective effects of the drug observed in animal models of acute myocardial ischemia and, in theory, could also serve to protect the myocardium of patients with hypertension, coronary artery disease, and congestive heart failure, in which oxidative stress is now recognized to occur. The antioxidant effects of carvedilol may both inhibit the direct cytotoxic actions of reactive oxygen radicals and prevent oxygen-radical induced activation of transcription factors and genes associated with inflammatory and remodeling processes. Accordingly, carvedilol inhibits the gene expression of the intracellular adhesion mol.-1 (ICAM-1), an adhesion mol. for polymorphonuclear leukocytes, which typically infiltrate the myocardium under conditions of ischemia and may exacerbate ischemic injury. The antioxidant activity of carvedilol has been shown to inhibit the oxidation of low d. lipoprotein (LDL) in vitro, thereby preventing the formation of this cytotoxic and atherogenic form of LDL. It follows, therefore, that in animal models of hyperlipidemia, carvedilol attenuates aortic lipid accumulation and decreases the aortic content of

L5 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

monocytes and foam cells, and at the same time it has been shown to preserve endothelial integrity and function. These actions of carvedilol are not shared by other beta-blockers or by other drugs currently used in the management of hypertension, coronary artery disease, or congestive heart failure. The multiple actions of carvedilol may provide the underlying pharmacol. rationale for the use of this drug in the treatment of patients with coronary artery disease or congestive heart failure, and these actions may account, at least in part, for the redn. in mortality produced by carvedilol in clin. trials involving patients with congestive heart failure. Likewise, these actions of carvedilol may also provide protection, beyond that afforded from redn. in blood pressure, against secondary organ damage in hypertensive patients treated with the drug.

IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol use in hypertension, coronary artery disease, and congestive heart failure in humans and laboratory animals)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

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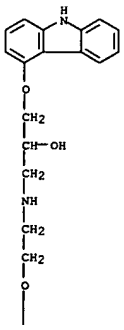

L5 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

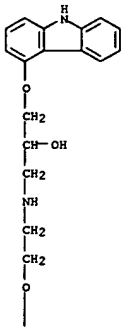
L5 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:964214 CAPLUS
DOCUMENT NUMBER: 124:75193
TITLE: Carvedilol update III: rationale for use in congestive heart failure
AUTHOR(S): Feuerstein, Giora Z.; Poste, George; Ruffolo, Robert R.
CORPORATE SOURCE: SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406-0939, USA
SOURCE: Drugs of Today (1995), 31(Suppl. F), 1-23
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 103 refs. In Feb. of 1995, several multicenter, double-blind, placebo-controlled clin. trials of the novel, multiple action cardiovascular drug, carvedilol, were terminated prematurely for ethical reasons due to the remarkable reduction in mortality observed in patients receiving carvedilol plus conventional therapy (i.e., angiotensin converting enzyme inhibitors, diuretics and digitalis) compared to patients receiving placebo plus conventional therapy. The dramatic reduction in mortality produced by carvedilol occurred across all studies and was observed in patients with mild, moderate and severe heart failure. The results of these dramatic clin. trials with carvedilol will be presented later this year. The purpose of this update is to describe in detail the multiple pharmacol. actions of carvedilol that make this drug unique, and which provide the rationale for its use in congestive heart failure. Carvedilol is both a β-blocker and a vasodilator, and these activities produce significant redns. in myocardial work and reduce all three parameters of myocardial oxygen demand, namely heart rate, contractility and wall tension. The vasodilatory effects of carvedilol reduce afterload, and the resulting decrease in impedance to left ventricular ejection offsets the neg. inotropic effect resulting from β-blockade, and as a result, stroke volume and cardiac output are maintained or even increased in patients with congestive heart failure. Carvedilol and several of its metabolites are extremely potent antioxidants, and this activity may account for the dramatic cardioprotective effects observed in animal models, and may also protect the myocardium of patients with congestive heart failure where oxidative stress is now recognized to occur. The antioxidant effects of carvedilol may inhibit both the direct cytotoxic actions of reactive oxygen radicals as well as preventing oxygen radical-induced activation of transcription factors and genes associated with inflammatory processes and cardiac remodeling. Accordingly, carvedilol inhibits the gene expression of ICAM-1, a critical adhesion mol. for polymorphonuclear leukocytes which typically infiltrate the myocardium under conditions of ischemia and exacerbate ischemic injury. These unique actions of carvedilol are not shared by any other drugs currently used in the management of congestive heart failure, or by any other β-blockers. The multiple.

IT 72956-09-3, Carvedilol
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(carvedilol update III: rationale for use in congestive heart failure)

L5 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

PAGE 1-A



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L5 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:440091 CAPLUS
DOCUMENT NUMBER: 117:40091
TITLE: Carvedilol, a new β-adrenoceptor antagonist and vasodilator antihypertensive drug, inhibits superoxide release from human neutrophils
AUTHOR(S): Yue, Tian Li; McKenna, Patrick J.; Ruffolo, Robert R., Jr.; Feuerstein, Giora
CORPORATE SOURCE: Dep. Pharmacol., SmithKline Beecham Pharm., King of Prussia, PA, 19406-0939, USA
SOURCE: European Journal of Pharmacology (1992), 214(2-3), 277-80
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carvedilol produced a dose-dependent inhibition of superoxide (O2-) release from human neutrophils (PMNs) (IC50 = 28 μM) and scavenged O2- generated during dihydroxyfumaric acid (DHF) autoxidn. (IC50 = 41 μM). Other β-blockers, such as celiprolol, labetalol and atenolol, or the antioxidant, 'lazaroid', U74500A had no effect on O2- either released from PMNs or generated during DHF autoxidn. Propranolol, at 0.3 mM, inhibited O2- release from PMNs (73%) but failed to scavenge O2- generated from DHF. The novel free radical-scavenging effect of carvedilol may contribute to the cardioprotective activity of the compound

IT 72956-09-3, Carvedilol
RL: BIOL (Biological study)
(superoxide release by human neutrophils inhibition by)
RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]-(9CI) (CA INDEX NAME)

L5 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

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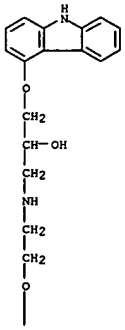

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L5 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:187811 CAPLUS
DOCUMENT NUMBER: 116:187811
TITLE: Cardioprotective effects of the vasodilator/beta-adrenoceptor blocker, carvedilol, in two models of myocardial infarction in the rat
AUTHOR(S): Smith, E. F. III; Griswold, D. E.; Hillegass, L. M.; Slivjak, M. J.; Davis, P. A.; DiMartino, M. J.
CORPORATE SOURCE: Dep. Pharmacol., SmithKline Beecham, King of Prussia, PA, 19406, USA
SOURCE: Pharmacology (1992), 44(6), 297-305
CODEN: PHMGBN; ISSN: 0031-7012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this study was to evaluate the cardioprotective effects of carvedilol, a β-adrenergic blocker and vasodilator, in two models of ischemic myocardial damage in the rat. Following coronary artery occlusion for 0.5 h and reperfusion for 24 h (MI/R group), left ventricular (LV) injury was determined by planimetric anal. of triphenyltetrazolium chloride-stained tissue, and polymorphonuclear leukocyte infiltration was assessed by measuring myeloperoxidase (MPO) activity. In the vehicle-treated MI/R group, infarct size was 14.2 of the LV, and MPO activity was increased to 2.8 from 0.14 U/g tissue in the vehicle-treated sham-occluded group. Carvedilol (1 mg/kg i.v., 15 min prior to coronary artery occlusion and at 3.5 h following reperfusion) reduced myocardial infarct size to 7.5% of the LV (n = 14) and attenuated the increase in MPO activity to 1.4 U/g tissue. A lower dose of carvedilol (i.e. 0.3 mg/kg i.v.) did not limit myocardial infarct size or the increase in MPO activity. In a model of permanent coronary artery occlusion, 24-h survival was reduced from 85% in sham-occluded animals to 44% in the vehicle-treated MI group. In comparison to the vehicle-treated MI group, carvedilol (0.3 mg/kg i.v., 15 min prior to coronary artery occlusion and 1 mg/kg 4 h after occlusion) improved survival by 55%, whereas the same dose of propranolol had no significant effect on survival. These results indicate that carvedilol reduces myocardial ischemia/reperfusion injury, and significantly improves survival in a permanent coronary artery occlusion model of myocardial infarction.

IT 72956-09-3, Carvedilol
RL: PRP (Properties)
(cardioprotective effects of, in myocardial infarction)

RN 72956-09-3 CAPLUS
CN 2-Propanol, 1-(9H-carbazol-4-yloxy)-3-[[2-(2-methoxyphenoxy)ethyl]amino]- (9CI) (CA INDEX NAME)

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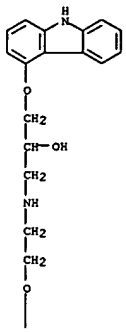

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FULL ESTIMATED COST                                   191.48     358.63

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -27.75     -27.75

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